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REGULAR DEPARTMENTS

A. M. A.
Archives of Neurology and Psychiatry

VOLUME 81 JUNE 1959 NUMBER 6

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Proceedings of a Symposium on Experimental "Allergic" Encephalomyelitis and Its Relation to Other Diseases of Man and Animals

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CONTRIBUTORS: 60 investigators from all over the world—distinguished for significant work in pathology, immunology, neurology, and biochemistry.

- *They examine critically whether any or all of these can really be considered due to allergic reaction.*
- *They evaluate the possible relation of these disorders to each other and to other diseases, such as multiple sclerosis.*

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Discussions built around twelve prepared speeches represent the heart of the book. **Authorities in other fields,** including most of those who have contributed to our knowledge of these diseases as well as many who are relatively unbiased by personal work in the field, participated. The discussions of each paper are recorded verbatim, edited to make readable, and brought up to date by many of the conferees since the symposium.

Here is the **newest information** concerning the etiology and pathogenesis of "allergic" encephalomyelitis, both as produced in experimental animals by injection of brain-containing vaccines and as occurring in man following injection of rabies-vaccine or other vaccines and following exanthematous or other infections.

Edited by

MARIAN W. KIES, Ph.D.
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Laboratory of Clinical Science
National Institute of Mental Health
Bethesda, Maryland

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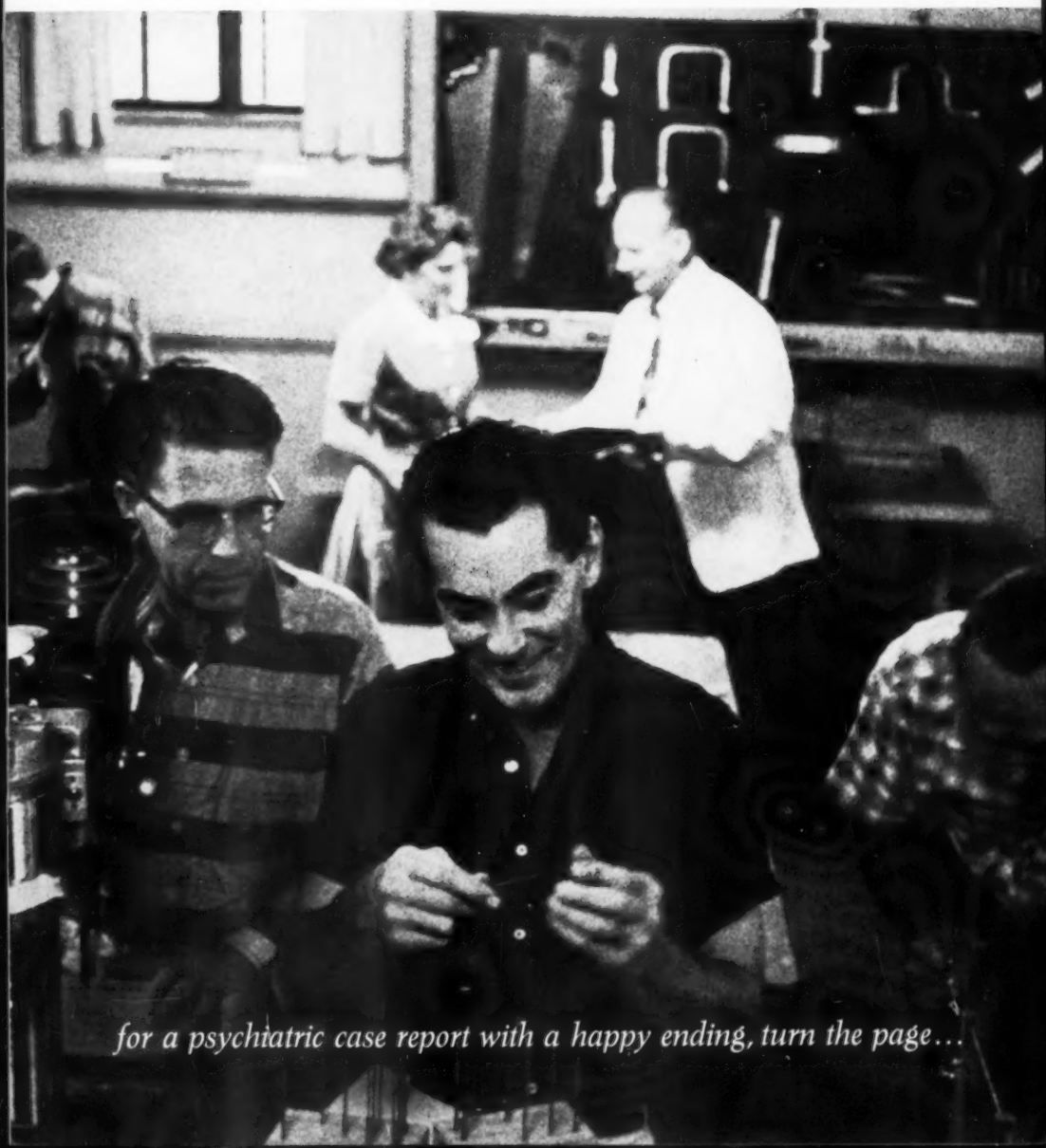

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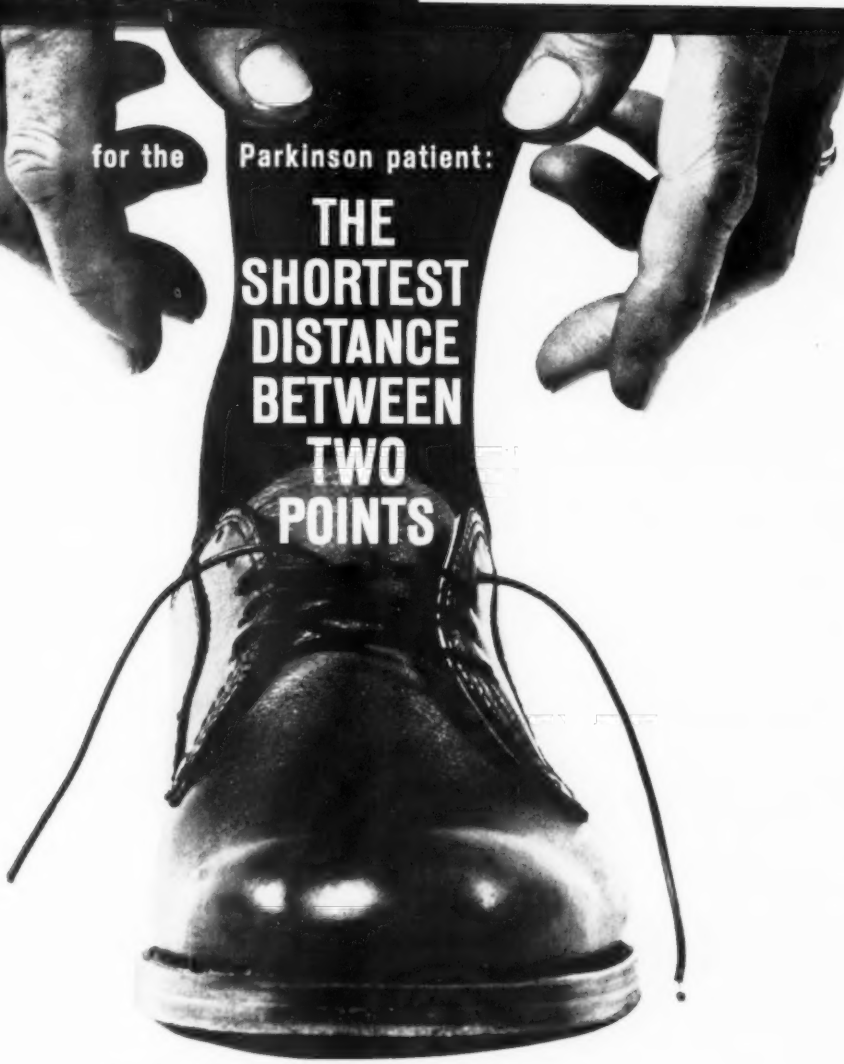

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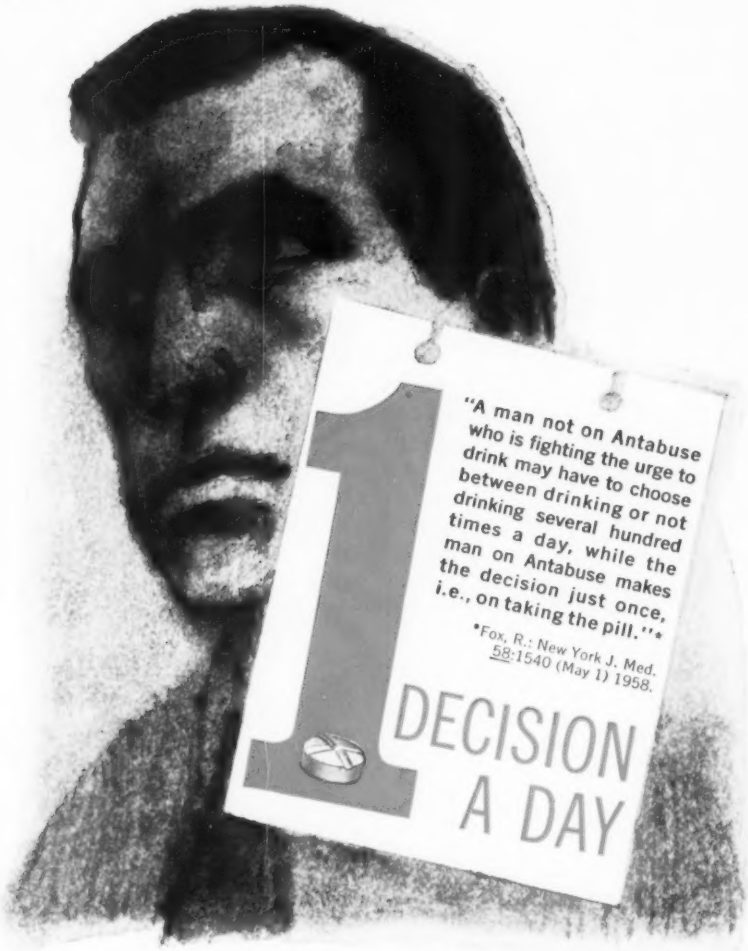

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by disease

DIAGNOSIS	NO. OF PATIENTS	NO. IMPROVED
SCHIZOPHRENIA		
PARANOID	7	2
NON-PARANOID	45	34
DEPRESSION		
PSYCHOTIC†	37	25
NEUROTIC	16	10
ANXIETY STATE	9	8
CHARACTER DISORDERS	15	13
OTHERS	16	13
TOTALS	145	105

by symptom

SYMPTOM	NO. IMPROVED
SLEEP DISTURBANCES	36
ANXIETY	30
TENSION	31
AGITATION	8
OTHERS	11
TOTAL	116

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SECTION ON
NEUROLOGY

Cerebral Embolism

The Natural History, Prognostic Signs, and Effects of Anticoagulation

CHARLES E. WELLS, M.D., New York

With the knowledge that anticoagulant drugs were effective in significantly reducing the incidence of cerebral embolic phenomena [1,2] and the evidence that in animals anticoagulants might increase the severity of experimental hemorrhagic infarcts,[3-5] the study of cerebral embolic phenomena in man has taken on new importance. This paper examines three aspects of cerebral embolism in man—the usual clinical course, the prognostic signs of significance, and the effects of anticoagulation upon the clinical outcome.

I. The Natural History

The present study is an effort to delineate the clinical features and course of cerebral embolic phenomena. In previous pathological studies [6,7] the natural history of those episodes ending in death has been considered, but this hardly gives a verisimilitude of the usual clinical course.

The records of 185 patients with a diagnosis of cerebral embolism admitted to the New York Hospital over the past 18 years were critically assayed. In 82 of these patients the diagnosis of cerebral embolism was definitely established by most stringent criteria. In view of the questions now surrounding the effects of anticoagulant therapy on cerebral embolic phenomena, the 29 patients so treated were excluded from this portion of the study, whose aim is to investigate the natural course of this disease process. Thus, 53 patients, with 63 episodes, were available for a more detailed clinical evaluation. The therapy in all these patients had been quite similar—rest, adequate supportive measures, physical therapy, and rehabilitation.

Diagnostic Criteria.—A diagnosis of cerebral embolism was made on patients under the age of 50 who had a cerebrovascular accident of sudden onset in the presence of rheumatic heart disease or embolic phenomena elsewhere without evidence of blood in the subarachnoid space. It was made on patients over the age of 50 who had a cerebrovascular accident of sudden onset in the presence of auricular fibrillation, recent changes in cardiac rhythm, or evidence of multiple embolic phenomena and without evidence of blood in the subarachnoid space.

Thus, a diagnosis of cerebral embolism was made in 36 patients under the age of 50 (Table 1). Thirty-two of these patients had rheumatic heart disease. Twenty-nine of these 32 presented other, more apposite historical factors or clinical findings which made the diagnosis of cerebral embolism more certain—auricular fibrillation, other embolic phenomena (within the brain or elsewhere), bacterial endocarditis, recent changes in cardiac rhythm, or recent cardiac surgery. Seventeen presented evidence of

Received for publication Aug. 12, 1958.

From the Department of Medicine (Neurology) of The New York Hospital and Cornell University Medical College.

TABLE 1.—*Diagnostic Criteria* *

Patients less than 50 years of age		36
Patients with rheumatic heart disease	32	
RHD+AF	10	
RHD+AF+other emboli	5	
RHD+other emboli	3	
RHD+other emboli+SBE	4	
RHD+SBE	3	
RHD+other emboli+postop	1	
RHD+AF+postop	1	
RHD+AF+recent change in rhythm	1	
RHD+recent change in rhythm	1	
RHD alone	3	
Patients without rheumatic heart disease	4	
Cooley's anemia+AF+other emboli	1	
Myxoma+other emboli	1	
HCVD+AF+other emboli+recent change in rhythm	1	
ASHD+other emboli+recent myocardial infarction	1	

TABLE 2.—*Sources of Cerebral Embolism*

Patients over 50 years of age		17
Rheumatic heart disease	5	
RHD+AF+other emboli	4	
RHD+AF	1	
Arteriosclerotic Heart Disease	3	
ASHD+AF+other emboli	1	
ASHD+AF	1	
ASHD+other emboli+recent myocardial infarct	1	
Hypertensive cardiovascular disease	4	
HCVD+AF+other emboli+recent change in rhythm	1	
HCVD+AF	3	
Myxoma	1	
Idiopathic AF	1	
Idiopathic AF+recent change in rhythm	1	
Fat emboli	1	
Septic emboli	1	

* RHD=rheumatic heart disease; AF, auricular fibrillation; SBE, septic bacterial endocarditis; HCVD, hypertensive cardiovascular disease; ASHD, arteriosclerotic heart disease.

multiple embolic phenomena—repeated cerebrovascular accidents; femoral, popliteal, or brachial artery occlusions; splenic infarcts, and renal infarcts. Those patients with bacterial endocarditis, of course, demonstrated multiple minute embolic phenomena in the skin, mucous membranes, and retinas. Three patients had sudden cerebrovascular accidents in a setting of rheumatic heart disease without the other cardiovascular involvements mentioned above. In these three there was no evidence of hypertension or diffuse vascular disease and nothing by history to suggest cerebral hemorrhage. Their spinal fluids were clear. A source of embolism was later demonstrated at autopsy in one of these.

A diagnosis of cerebral embolism was made in 17 patients over the age of 50, in all of whom auricular fibrillation, multiple embolic phenomena, or a source of emboli was demonstrated. Details are given in Table 2.

Seventeen episodes occurred while the patients were in the hospital for other causes. The other patients were hospitalized because of their embolism, nearly all on the day of onset. None are included who were hospitalized seven or more days after onset.

Observations.—Sixty-three separate episodes of cerebral embolism were observed in 53 patients. There were 33 (62%) women with 41 (65%) episodes and 20 (38%) men with 22 (35%) episodes. Ages ranged from 3 to 76 years, with the highest incidence in the fourth and fifth decades of life.

Cardiac Status: Thirty-seven (70%) of the 53 patients suffered from rheumatic heart disease, and 9 (17%), from hypertensive or arteriosclerotic vascular disease. Two had auircular fibrillation of unknown cause, and two had myxomas of the left auricle.

In three of the patients with rheumatic heart disease the episode of cerebral embolism occurred at or just after cardiac surgery for correction of mitral stenosis. Seven patients (13%) had bacterial endocarditis (six subacute, one acute) at the time of embolism, and in four this was proved by culture or autopsy.

In 25 (47%), including the 7 just mentioned with bacterial endocarditis, examination revealed normal sinus rhythm following the cerebral emboli episode. Nevertheless, in this group there was evidence of multiple embolic episodes in 11, evidence of recent changes in cardiac rhythm in 5, and demonstration of a source of emboli in 9 in whom autopsy was performed.

Of the five patients with known recent changes in cardiac rhythm, one had been given quinidine to convert an idiopathic

TABLE 3.—*Hour of Onset of Cerebral Embolism*

Hour of Onset	Number
6 a. m.-12 a. m.	25 (61%)
12 a. m.- 6 p. m.	6 (14.5%)
6 p. m.-12 p. m.	3 (7.5%)
12 p. m.- 6 a. m.	7 (17%)
	41 (100%)

auricular fibrillation to normal sinus rhythm, the conversion having occurred two days previously. None of the others gave a history of recent iatrogenically induced changes in rhythm.

Repeated Emboli: Twenty patients (38%) gave a history of previous embolic episodes which had occurred before they were observed at this hospital for a cerebral embolus. Of these, 8 had had previous cerebral emboli; 11, extracerebral emboli, and 1, both forms. In 33 (62%) the cerebral embolus was the first known embolic episode. Seven had other embolic episodes within the month before or the month following the cerebral embolus.

Onset: The onset occurred most frequently in the morning hours. The time of onset could be ascertained with reasonable accuracy in 41 episodes (Table 3).

The situation at the onset could be determined in 45 instances. The majority of episodes (67%) occurred while the patients were either sitting quietly or lying in bed. Seven patients awoke to discover their incapacity. In only six was there any association with physical effort other than the mildest variety.

Only seven patients (13%) gave a history of "warning" symptoms. These are listed in Table 4. The onset was manifested by a convulsive seizure in eight instances (12.5%). Six of these seizures were major generalized attacks, and two were focal seizures which did not progress to generalized seizures. Loss of consciousness was a manifestation of onset in 19—in 7 of these for only a few minutes or less.

Headache was a significant feature of the onset in 14 patients, with 16 (25%) episodes. In four episodes it was described as being of slight to moderate severity, but in seven it was specifically described as being of high intensity. It was most frequently throbbing in character and diffuse or bifrontal in location. In five patients the pain was more localized, maximal over the hemicranium.

TABLE 4.—*Warning Symptoms of Cerebral Embolism in Seven Patients*

Patient	Warning
1	10-15 min. period of transient numbness of right arm and leg with feeling of speech being "off" 24 hr. before onset; severe frontal headache and vomiting 12 hr. before onset of right hemiparesis
2	Episode of "lightheadedness" of a few minute's duration two days before onset
3	Severe throbbing bifrontal headache with nausea and vomiting for 8 hr. before onset of visual loss
4	Felt "unwell" for 1 hr. before onset of weakness and loss of consciousness
5	Awoke feeling less cheerful than usual and complaining of dull right parietal headache 3 to 4 hr. before onset of left hemiparesis
6	Severe right occipital headache for one day before onset of weakness
7	Severe pulsating frontal headache for 2 wk. before onset

Three patients noted vertigo at the onset. Nausea and vomiting occurred in four patients, in three in association with headache. Four patients complained of visual loss at the onset. In three of these hemianopsia was found. The fourth stated that the left eye was "blurry in vision," but no visual loss was found on admission two and one-half hours later.

Symptoms and Signs: The vital signs were generally not significantly altered. The neurological signs were those which might be expected from any focal lesion within the cranium, and there is no necessity for discussing these in detail. The lesion appeared to involve the left cerebral hemisphere in 18 instances, the right in 32 instances, and the brain stem in 5. It was bilateral in three, and in five the precise localization could not be determined. It is of interest that nine patients with evidence of an upper motor neuron type of hemiparesis also showed significant degrees of weakness of the upper facial musculature on the paretic side. Seven showed Cheyne-Stokes respirations at some time in their

course. Speech impairment was noted in 20 episodes. Twelve patients exhibited aphasia; all save one of these had associated right hemiparesis.

Laboratory Findings: In general, the results of laboratory examinations were nonspecific. The total white blood cell counts done within 48 hours of onset varied from 7,600 to 34,400. In 11 the WBCs were over 15,000 and in 4 over 20,000 (only one in a patient with bacterial endocarditis). Differential counts showed an average of 65% polymorphonuclear leukocytes, 14.7% band forms, and 16% lymphocytes.

Lumbar puncture was performed in 31 patients at varying times up to 24 days after onset. It was performed in 21 patients within 72 hours of onset. The opening pressure was recorded in 20 of these patients and was within normal limits (180 mm. being accepted as the upper limits of normal) in 18. Two patients showed elevation of pressure; one of these had bacterial endocarditis, with considerable cellular reaction. The fluid was crystal clear and colorless in 20. Except for the patient with bacterial endocarditis whose cerebrospinal fluid showed 2,500 RBC/cu. mm. and 800 WBC/cu. mm. (80% lymphocytes), only two patients revealed over 5 RBC/cu. mm. (10 and 9/cu. mm., respectively) or over 5 WBC/cu. mm. (7 and 11/cu. mm., respectively).

In this group the cerebrospinal fluid protein was elevated above 45 mg. % in six (32%); above 57 mg. % in only two: to 81 mg. % in one patient and to 100 mg. % in a patient with bacterial endocarditis. The Pandy response was negative or "trace"-positive in the 12 patients on whom it was performed.

In considering this entire group of 31 patients, the only striking abnormalities of cellularity were in those who had bacterial endocarditis. Likewise, the only cerebrospinal fluid protein over 100 mg. % was in a patient with bacterial endocarditis.

Electroencephalograms were obtained on only eight patients, too small a number for meaningful evaluation.

Episodes of Cerebral Embolism: Sixteen patients (30%) had more than one episode of cerebral embolism. Nine of these were observed during repeated episodes of cerebral embolism; and seven gave a clinical history entirely compatible with a previous cerebral embolic episode. Ten patients by history or by observation had recurrent episodes of strikingly similar clinical pattern in each episode, whereas six patients had multiple episodes involving different portions of the central nervous system.

In the nine patients whose recurrences of cerebral emboli were observed, the shortest period between successive episodes were 6 and 17 days (the former in a patient with Cooley's anemia with multiple diffuse embolic episodes).

Outcome: Sixteen patients (25%) died as a direct result either of the cerebral embolus or of its complications within two and one-half hours to two months following onset of the illness (two had associated endocarditis). Five died within 24 hours of onset. Twelve died within one week of onset.

Twenty-two (35%) of the episodes resulted in significant amounts of residual dysfunction. There was severe hemiparesis in 20 patients, speech impairment in 8, evidence of mental deterioration in 5, and seizures, diplopia, and hemianopsia, 1 instance each.

Following 25 episodes (40%) there was only minimal or no neurological deficit. In 13 episodes complete recovery followed, and in 12 the residual dysfunction was only very slight. After eight of these there was minimal motor paresis, and after four, slight speech dysfunction.

Autopsy Findings: Autopsy was performed on six patients who died as a result of the cerebral embolus. In three the embolus itself was identified; in two the cerebral infarcts were hemorrhagic and the embolus per se was not seen, but there were multiple emboli elsewhere, and in one the pathological examination was inadequate. Autopsy was performed in nine patients who died later of causes other than the embolus (in one, permission for examina-

tion of the brain was refused). Seven of these showed old anemic brain infarcts, and one showed the embolus itself. Either multiple embolic phenomena or a source for embolism was identified in six of the nine, including the one whose brain was not examined.

Comment.—Embolism has been regarded for many years as a major cause of cerebral vascular accidents [6-10]; yet many gaps remain in our knowledge of the clinical course of this disease.[7] Harris and Levine [11] have studied cerebral embolism as a clinical phenomenon specifically, but only in a group having mitral stenosis. The present study attempts to give a clearer concept of the usual clinical features of this disorder.

As has previously been stressed, almost all the patients of this present series had evidence of heart disease providing a ready source of emboli. In contrast to earlier studies, only 13% of these patients had vegetative endocarditis associated with their embolism. Thus, Aring and Merritt,[6] in 1935, found vegetative endocarditis in 43% of patients dying of embolism. This doubtless represents the change in course of endocarditis since the onset of antibiotic therapy.

It was surprising to discover in the course of the present study that 47% of the episodes occurred in the presence of normal sinus rhythm. Eleven of these also had evidence of multiple embolic phenomena, and nine, autopsy proof of sources of emboli, thus emphasizing that fibrillation is not the *sine qua non* for arterial embolism.[12,13] Harris and Levine [11] previously had found normal sinus rhythm in 23.6% of their patients with mitral stenosis having cerebral embolism.

Although it has been said that cerebral embolism is "not preceded by prodromal cerebral symptoms," [8] Merritt [14] has called attention to frequent prodromal symptoms, notably headaches and vomiting; and Fisher [15] has mentioned the "stuttering" onset of symptoms. In the present series there were warning symptoms in 13% of the episodes. It is difficult to explain the basis of such a warning, since the effects of an embolus are supposedly due to occlusion of a vessel. Perhaps the embolus first causes partial occlusion giving the prodrome, the symptoms of the accident itself occurring when the embolus finally becomes lodged and completely occludes the vessel (as suggested by Fisher [15]). It is hard, though, to conceive why this halting course through the extent of a vessel should occur.

Whereas the time of onset was not significant in Aring and Merritt's series, in 61% of the episodes of this series in which the time of onset could be accurately ascertained, it occurred between 6 a. m. and noon. This might suggest that the transition from the resting metabolic level of sleep to the active level of waking is significant in precipitating embolism. In sedentary patients such as these, this transition might well be the most strenuous activity of the day.

Seizures occurred at the onset in 12.5%, or with approximately the same frequency as that given by Merritt.[16,17] Headache occurred in 25%, approximately the same as reported in other studies.

While it is doubtless true, as Aring and Merritt [6] have stated, that the occurrence of severe headache at the onset strongly suggests a diagnosis of cerebral hemorrhage, a severe headache may appear at the onset of cerebral embolism as well, as occurred in 11% of the present series of episodes. This headache may be due to the embolus being lodged in the pain-sensitive vessels at the base of the brain or to edema-producing traction displacement of pain-sensitive venous channels.

The laboratory examinations may be of value in helping to confirm the diagnosis and to help in ruling out other possible diagnoses. A mild leukocytosis is usually seen. Although it has been said that a leukocyte count of over 20,000 is diagnostic of a cerebral hemorrhage unless there is infection,[17] four patients in this series had WBCs of over 20,000/cu. mm., and in only one was infection present.

The 16 patients who died as a result of the cerebral embolism survived from two

and one-half hours to two months after onset, thus adducing further evidence that cerebrovascular accidents rarely cause sudden death.[17] The 25% mortality figure in this series is comparable to the 33% mortality rate in the series of Harris and Levine.[11]

Summary.—The clinical course of 63 episodes of diagnosed cerebral embolic phenomena in 53 patients is analyzed.

Seventy per cent of the patients had rheumatic heart disease, and 17%, hypertensive or arteriosclerotic heart disease.

Forty-seven per cent had normal sinus rhythm.

The onset was most frequent in the morning hours. Headache was a feature of onset in 25%, and seizures, in 12.5%.

The laboratory findings were nonspecific.

Thirty per cent of the patients had more than one episode of cerebral embolism.

Twenty-five per cent of the episodes ended in death, and 35% resulted in severe permanent neurological dysfunction.

II. Prognostic Signs

In this portion an attempt is made to analyze the clinical picture of the patient with cerebral embolism when seen in the first few hours of illness to determine whether any prediction of the eventual outcome may be made at that time. In other words, this study seeks to answer the question "What will be the outcome in this patient who has had a cerebral embolus?" without the tedious procedure of awaiting the unfolding of the full clinical course.

It was immediately obvious that the apparent severity of disability manifested at the onset was no guide to the ultimate prognosis, since nearly every patient appeared severely impaired at the time of onset. Many with profound hemiparesis made a speedy and complete recovery, while in others severe impairment persisted. What other factors, then, could help in predicting the result?

For the purpose of this study, the results of cerebral embolic episodes have been divided into two groups: (1) good results, comprising 24 episodes which left little or no residual; i. e., the patient was able to continue the same activities as he did prior to the embolic episode; (2) poor results, comprising 39 episodes, which resulted either in severely impaired function or in death. An evaluation is made of which factors can be correlated with the first group and which with the second.

Observations.—Age: The age of the patient at the time of the episode appeared to have some relation to the eventual outcome. In patients over 50 years of age 15 of 18 episodes (83%) gave poor results; in patients under 50 years of age only 24 of 45 (53%) fell into this second group.

Of 37 patients with rheumatic heart disease, 25 either died or had severe residuals in 44 episodes of cerebral embolism, while 8 of 9 patients with hypertensive cardiovascular disease or arteriosclerotic heart disease had similar results. Thus the outcome was considerably less felicitous in those patients with hypertensive cardiovascular disease or arteriosclerotic heart disease than in those with rheumatic heart disease. Of the episodes occurring in patients with bacterial endocarditis, four of nine fell into the second group.

Repeated Emboli: An attempt was made to determine whether repeated episodes of cerebral embolism were more likely to result in death than the first cerebral embolus. Not all the earlier episodes had been observed. Forty-two episodes were observed which were thought to be the first cerebral embolism in the individual patient; of these, 10 were fatal. Of 15 patients observed in their second episode, 4 died and of 3 observed in their third or fourth cerebral embolic episodes, 1 died. In three the exact number of clinical episodes could not be determined.

Symptoms and Signs: Of the seven patients having episodes preceded by warnings, five had poor results. In 10 of 16 episodes in which headache was a symptom, the outcome was poor. Seven of eight episodes in which the onset was accompanied

by seizures resulted either in death or in severe disability.

Of 20 episodes in which loss of consciousness occurred, only 3 had a good outcome. Only one patient who was comatose for over three hours survived the episode.

Speech impairment (either slurring or aphasia) occurred in 19 episodes, 12 of which resulted in death or severe disability. There was no significant difference in prognosis as regards motility and sensory function whether the embolus went to the right or the the left cerebral hemisphere, though no special studies were done to ascertain the effects of aphasia on over-all adaptation. Both upper and lower facial weakness on the hemiparetic side was noted in nine episodes; six of these were placed in the second group. The Cheyne-Stokes type of respiration occurred in seven episodes; six of these ended with death and one with severe residuals.

In 13 episodes there followed a significant increase in the extent or severity of disability over that reached at the time of onset. Only 4 of these 13 episodes evincing progression of debility failed to terminate in death, and only 1 ended without severe effects.

Laboratory Findings: Of the 12 patients with initial white blood cell counts over 15,000/cu. mm., the results in 9 were poor. Of those under 15,000/cu. mm., results in 18 of 29 were similar. No relation between spinal fluid findings and outcome could be found.

Recovery: Of the 9 instances in which recovery of strength began less than 12 hours after onset, only 1 terminated with significant residua; and of the 20 in which recovery began less than 24 hours after onset, only 4 had poor results. When recovery began 24-48 hours after onset, one of the six had a similar outcome. When significant recovery started over 48 hours after onset, 18 of 22 terminated with poor results (Table 5).

TABLE 5.—*Beginning of Recovery and Outcome*

Results	Recovery Began Less Than 48 Hr. After Onset	Recovery Began More Than 48 Hr. After Onset
Good	21	4
Poor	5	18

Comment.—While it is obvious from these observations that no one point in the clinical history will allow prediction of the outcome of an individual episode of cerebral embolism, it is also apparent that a number of factors are likely to be incompatible with good recovery. A concatenation of these factors allows one to predict a poor termination with some degre of assurance.

The results in patients over the age of 50 and in those with hypertensive cardiovascular disease or arteriosclerotic heart disease are not as good as in patients under 50 and with other forms of disease. Which of these factors is most important is indefinite, since hypertension and arteriosclerosis usually occur in the older age groups.

Repeated embolic episodes appeared no more incompatible with survival than did the first episode.

Only two of seven patients in this series with warnings had good results. The uncertainity of the basis of this prodrome has already been discussed—whether it represents two embolic episodes, complete occlusion of what was previously a partial occlusion, or hemorrhage into an area of previously anemic infarction. Whatever its mechanism, those episodes preceded by warnings usually have a bad outcome.

Convulsive seizures are usually an ominous sign, only one of eight patients with seizures having escaped serious residual dysfunction or death. Loss of consciousness is a similarly poor prognostic sign, particularly when prolonged over a several-hour period, a factor previously noted by Tennent and Harman for other forms of cerebrovascular accidents. The appearance of Cheyne-Stokes respirations is likewise inauspicious, since good results occurred in none of the seven patients in whom this occurred, and indeed only one escaped death.

The occurrence of upper facial paresis, along with lower facial paresis on the

paretic side, was frequently accompanied by a poor result. This may perhaps indicate the severity of the paresis.

Any increase in symptoms or signs beyond those evident in the first few minutes after onset is a poor prognostic sign and unlikely to be associated with good recovery.

When recovery from the paresis begins less than 48 hours after onset, the chances for good recovery appear fairly promising. Only 5 of 26 episodes in this series in which recovery began less than 48 hours after onset resulted in severe dysfunction, whereas 18 of 22 in which recovery began later had poor results. Thus, if recovery from paresis has not begun 48 hours after onset, a poor result can be predicted with some certainty.

Summary.—An evaluation has been made of the results following 63 episodes of cerebral embolism in 53 patients, with the object of determining what factors, if any, allow prediction of a good or a poor result early in the course of illness. The occurrence of seizures, prolonged loss of consciousness, Cheyne-Stokes respirations, or a significant increase in signs or symptoms after the first few hours following onset was unlikely to be associated with good recovery in this series. If paresis did not begin to diminish within 48 hours after onset, the chance for good recovery was slight.

III. Effect of Anticoagulants upon the Clinical Course

Recent studies[3,5] have shown that following experimental cerebral embolism the area of hemorrhagic infarction is larger when the animal is given anticoagulants than when none are administered. These findings suggested that in man the prognosis for cerebral embolism might be much poorer when the patient was already receiving anticoagulants or when anticoagulants were begun immediately after the onset of the episode of cerebral embolism than when the patients was not receiving such medication. The present study attempts to ascertain whether the use of anticoagulants has any significant effect upon the clinical outcome of cerebral embolic phenomena. The beneficial role of anticoagulants in preventing thromboembolic episodes is not here questioned.

Only one previous paper has been found relevant to this problem in man. Carter,[19] in 1957, published observations on the effect of various modes of treatment of cerebral embolism. He found no difference between the untreated, control group and the group receiving stellate ganglion block, but he did find that a significantly higher number of patients recovered when anticoagulants were given soon after the embolic episode than when no anticoagulants were given. He also noted a significant reduction in mortality in the group treated with anticoagulants. Ushiro and Schaller[20] did not differentiate between embolic and thrombotic episodes in their study of the effects of anticoagulants on cerebrovascular accidents.

Clinical Material.—This study compares the results in 53 patients having 63 episodes to whom no anticoagulants were administered with the results in 29 patients having 34 episodes who either were receiving anticoagulants at the onset of the episodes (13 patients) or were started on this therapy within 48 hours after onset. Except for the administration of anticoagulants, the treatment received by the two groups of patients was entirely comparable.

Because of the well-known hazards of retrospective studies, every effort was made to ascertain that these two groups were indeed entirely comparable except for administration of anticoagulant drugs. Those already receiving anticoagulants were doing so because of previous embolic episodes. Those for whom anticoagulants were begun immediately were so treated because of the conviction of the physicians responsible for the patient's care. The medical service had established no specific policy regarding the use of anticoagulants for cerebral emboli.

The treated group contained 20 women (69%) and 9 men; the untreated group included 33 women (62%) and 20 men. The mean age of the treated group was 50 years and that of the untreated group was

TABLE 6.—*Incidence of Seizures, Loss of Consciousness, and Cheyne-Stokes Respiration in Two Groups*

	Total Episodes	Seizures		Prolonged Loss of Consciousness		Cheyne-Stokes Respirations	
		No.	%	No.	%	No.	%
Episodes without anticoagulants	63	8	12.5	12	19	7	11
Episodes with anticoagulants	34	5	15	3	9	3	9

45 years, the difference not being significant. In the treated group, 27 of 29 patients had rheumatic heart disease, whereas only 37 of 53 patients (70%) in the untreated group had this condition.

It has been shown that those patients whose episodes were manifested by seizures, prolonged loss of consciousness, or Cheyne-Stokes respirations were particularly likely to have a poor prognosis. As can be seen in Table 6, the differences in these features between the two groups is negligible. Thus, these two groups appear quite comparable in the nature and severity of their disease.

Within the treated group, 13 episodes occurred in patients who were already receiving anticoagulants because of previous embolic episodes. These patients were receiving ethyl biscoumacetate (Tromexan) or bishydroxycoumarin (Dicumarol) and were being followed in the Anticoagulant Clinic of the New York Hospital or by their private physicians. In 21 episodes anticoagulants were begun within 48 hours after onset (within 24 hours in all save 2). These patients were given varying types of anticoagulants (intravenous, intramuscular, or subcutaneous heparin; oral ethyl biscoumacetate, or oral bishydroxycoumarin), with no one method predominating. The method of choice rested with the physician directly in charge of the patient's care.

Results.—Among the 63 episodes occurring in patients in the untreated group, 16 (25%) resulted in death; among the 34 episodes occurring in the group treated with anticoagulants, in only 2 (6%) did death occur (Table 7). Thus the death rate was significantly lower ($P<0.05$ by Fisher's table) in the treated group than in the untreated group.

Among the 63 episodes occurring in the untreated group, 22 (35%) resulted in severe permanent disability; among the 34 episodes occurring in patients receiving anticoagulants, 13 (40%) resulted in severe permanent impairment of function. Thus, 38 of 63 (60%) untreated episodes resulted either in death or in permanent disability, and 15 of 34 (44%) treated episodes resulted either in death or in severe dysfunction. Therefore the results in the treated group, as measured by death and disability together, were also better than those in the untreated group, though the difference is not statistically significant ($P<0.20$).

Among the 13 patients receiving anticoagulants at the time of onset of their embolus, prothrombin time was known within a few days of onset in 11 instances. The prothrombin time was within normal limits in only one and was not above the therapeutic range in any. There was no obvious difference in the outcome between the group already receiving anticoagulants and that which was begun on anticoagulants immediately after the accident. The methods of immediate anticoagulation were so varied that no adequate comparison can be made among them as to the efficacy of results.

TABLE 7.—*Relation of Outcome to Anticoagulant Therapy*

	Not Treated with Anticoagulants	Treated with Anticoagulants
Dead	16	2
Alive	47	32
Total	63	34

Lumbar punctures were performed in 17 of the 34 treated episodes, and in 6 there was a significant increase in the red blood cells in the cerebrospinal fluid (up to 67,000/cu. mm. in one patient with subacute bacterial endocarditis as well). This is in contrast with the findings in the untreated group. In three of these the red blood cells appeared in patients already receiving anticoagulants, and in three the red blood cells appeared after anticoagulant therapy had been begun. All except one of these with known cerebrospinal fluid bleeding resulted either in death or in severe disability.

Comment.—Although animal experimentation had suggested that anticoagulants might increase dysfunction secondary to cerebral embolism, the present study has failed to substantiate these expectations in man. An earlier study by Carter [19] suggested that morbidity and mortality from cerebral embolism were decreased when anticoagulants were begun just after the embolic episode. The present study confirms these findings in man, showing statistically significant decreased mortality in the treated group as compared with the untreated group. No evidence can be adduced from this study as to which method of anticoagulation gives best functional results, or whether anticoagulation before the accident gives better results than anticoagulation immediately after the accident.

The fact that severe disability resulted in those with bloody cerebrospinal fluid suggests that when significant intracranial bleeding does occur during anticoagulation the results are likely to be poor.

Why anticoagulation should decrease morbidity and mortality is difficult to understand, especially in view of the known frequency of hemorrhagic infarcts after embolism.[9] It may be that anticoagulation allows speedy recanalization and return of blood supply to the infarcted area, as suggested by the animal experiments of Wright, Kubic, and Hayden,[21] or perhaps, as Meyer [22] has recently shown in animals, anticoagulation promotes better collateral circulation by preventing local ischemia due to increased viscosity of the blood; but for neither of these explanation is there proof in man at present.

Thus the findings in this series do not confirm the suspicions aroused in earlier experimental studies that in cerebral embolism the results are likely to be poorer if prior or immediate anticoagulation is employed.

Summary.—A comparison is made between results in 63 episodes of cerebral embolism occurring in patients in whom no anticoagulants were given and in 34 episodes occurring in patients either already receiving anticoagulants or to whom anticoagulants were administered within 48 hours after onset. This comparison demonstrated a slight decrease in morbidity and a significantly reduced mortality in the treated group as compared with the untreated.

Conclusions

The clinical course following cerebral embolism is analyzed for a group of patients treated with anticoagulants and for a group not so treated. A poor prognosis was found for those patients in whom the onset was accompanied by seizures, prolonged loss of consciousness, or Cheyne-Stokes respirations; in whom a significant increase in signs or symptoms appeared in the first few hours following onset, or in whom improvement did not occur within 48 hours. In the untreated group, 25% of the episodes of cerebral embolism ended in death; in the treated group, 6% ended in death. Thus these findings do not confirm the view that anticoagulation in the presence of cerebral embolism in man might result in increased mortality and morbidity.

The physicians of the New York Hospital allowed me free use of the hospital records of their private patients and gave permission for the inclusion of these cases in this series for publication.

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Muscle Dystrophy in Mice of the Bar Harbor Strain

An Electromyographic Comparison with Dystrophia Myotonica in Man

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The presence of fibrillation in the muscles of the Bar Harbor strain of dystrophic mice has previously been reported from this laboratory.[1] We have observed that the electromyogram from dystrophic mice of this strain is strikingly similar to that recorded from muscles of patients suffering from dystrophia myotonica. The muscles of such patients and animals are hyperirritable, and the records obtained by the insertion of a concentric needle electrode reveal the presence of short motor volleys of high frequency against a background of electrical activity characteristic of denervated muscle. In order to demonstrate the presence of fibrillation, free of the superimposed activity from innervated structures, it was decided to study the electrical activity of muscles in dystrophic mice and patients in whom the motor nerves were blocked.

The identification of characteristics common to both the dystrophy in this strain of mice and a particular form of dystrophy in man was considered an important step in establishing the value of these animals for further comparative studies.

Method

Mouse.—Twenty dystrophic mice of the Bar Harbor strain, along with a similar number of normal litter mates as controls, were used. For electromyography the animals were anesthetized with a cyclopropane-oxygen mixture accurately controlled by means of special microflow meters.

Electrical activity of the gastrocnemius and muscles of the hindfoot was recorded by inserting a 27-gauge, concentric, single-core electrode. Action potentials were photographed on the face of a Dumont double-beam oscilloscope and also were recorded on magnetic tape. One oscilloscope beam provided a continuous trace (lower) at 28.2 mm. per second. The second beam provided a parallel, high-speed, interrupted trace (upper) consisting of single sweeps, triggered by the camera to record on adjacent frames at 1.5 to 2.0 mm. per millisecond. Action potentials were also continuously monitored on a loud speaker.

In each of two dystrophic mice one sciatic nerve was exposed in the thigh. The midsection of exposed nerve was supported on a narrow U of 17-gauge hypodermic needle tubing which was bent practically to encircle the nerve over a length of 3 mm. The metal tube was connected to flasks from which water at 0 or 37 C could be forced under pressure.

A Grass stimulator was used to deliver single-spike shocks at intervals of one second through a pair of electrodes on the nerve proximal to the cooling tube. Failure of the muscle to respond to indirect stimulation indicated when the nerve had been chilled sufficiently to produce block.

Man.—Seven dystrophic patients of both sexes with an age range from 6 to 53 years were studied electromyographically with a similar recording method. With two of the patients, procedures were used to minimize or block active innervation of motor units during the time of recording. One patient (Patient 6) with generalized, progressive muscular dystrophy, was brought to plane II surgical anesthesia with intravenous thiopental (Pentothal) sodium. On a second patient (Patient 2), classified as a typical case of dystrophia myotonica,*

* Patient 2, a white man, age 53, had a history of slowly progressive muscular weakness and atrophy since the age of 30, at which time he first noticed difficulty in relaxing his clenched hand. At present the patient exhibits weakness and moderately severe atrophy of muscles in all four extremities, the neck, and the face. There is marked difficulty in relaxation of hands after clenching a fist. Locomotion is limited to a four-point gait on crutches. Eyelid ptosis is prominent. Testes are small. The electromyogram exhibited numerous "dive-bomber" bursts typical of myotonia (Observation 4 of "Results").

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repeated studies were made, including one experiment as follows:

To establish the characteristic pattern of activity with innervation intact, an electrical record was taken from the ulnar muscle of each forearm and hand at rest, as well as during and following voluntary effort. With the concentric electrode in the abductor digiti quinti, the ulnar nerve was blocked at the medial condyle by the injection of 2% lidocaine (Xylocaine) hydrochloride. Eighteen minutes after the injection, when there was evidence of complete motor and sensory block, recording was continued.

Results

The following observations were repeatedly made upon both the dystrophic mice and the two patients with the myotonic form of dystrophy.

1. There was gross evidence of weakness and atrophy of involved muscles.

2. Vigorous movement (voluntary in man, reflex in mouse) was followed by prolonged tetanic contraction and very gradual relaxation.

3. The insertion of a concentric electrode and slight movement of the tip within a relaxed muscle aroused excessive electrical activity, characterized by repeated, high-frequency bursts of action spikes at 50 to 100 or more per second. The ease with which these could be elicited was in sharp contrast to the almost complete electrical silence upon insertion of a needle into normal relaxed muscles.

4. With the electrode motionless in a relaxed muscle there were frequent, spontaneous volleys of action potentials, which quickly reached frequencies over 50, and sometimes over 100, per second. These gradually diminished in frequency over a period of one to five or six seconds to a discharge rate of approximately 20 per second, when the volley would abruptly cease. Action potential voltages as recorded during these volleys often exceeded 250μv. at the beginning and progressively diminished, along with the rise and fall in frequency, to a terminal voltage approximately 30% of the original (Fig. 3).

5. Often with proper placement of the concentric electrode, single-action potentials

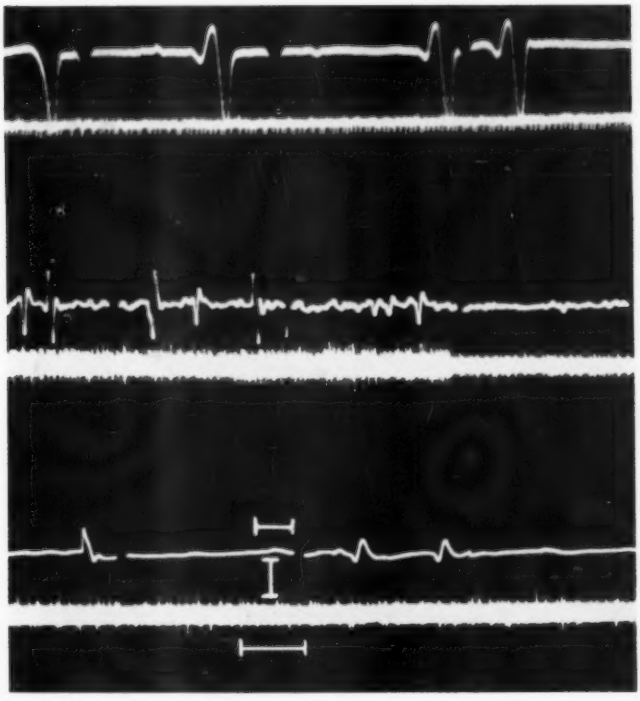

Fig. 1.—Mouse electromyograms: Upper, normal; middle, denervated; lower, dystrophic. Upper trace (of each pair) one sweep per frame; calibration bar=3 msec. Lower trace: continuous; calibration bar=1 sec. Vertical calibration bar=200μv (all traces).

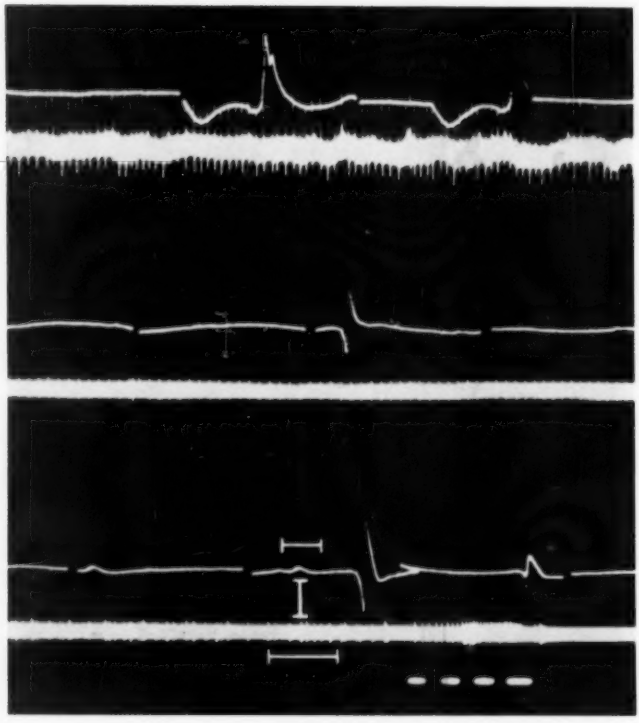

Fig. 2.—Human electromyograms: Upper, normal; middle, denervated; lower, dystrophic. Calibrations as for Figure 1.

were found to be repeating steadily at low frequencies (0.5 to 13 per second). These individual complexes were of short duration (0.8 to 1.8 msec.). The constancy of voltage and rate of repetition made it easy to identify these action potentials as arising from a single unit, presumably from a single cell. They were occasionally found to accelerate and decelerate slowly in rate of repetition. In every respect they were indistinguishable from the action potentials recorded in fibrillating denervated muscle (Figs. 1 and

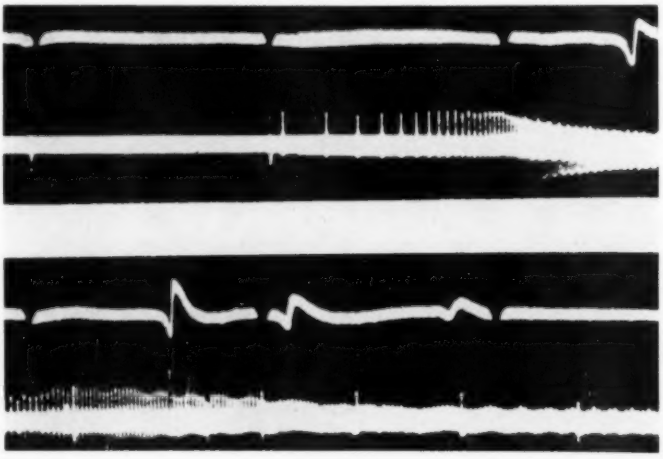

Fig. 3.—Electromyograms on Patient 2. (Dystrophia myotonica): Upper, before nerve block; lower, after nerve block. Calibrations as for Figure 1.

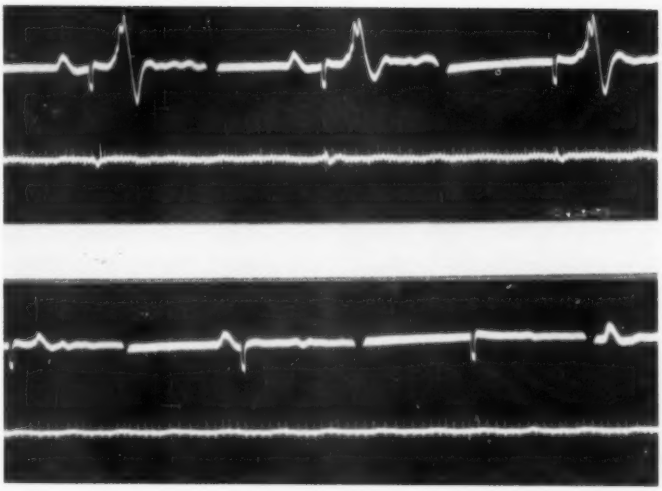

Fig. 4. — Electromyograms on dystrophic mouse (Bar Harbor strain) while muscle was indirectly stimulated. Upper, before nerve block; lower, after nerve block. Calibrations as for Figure 1. In the top trace the first complex is the slowly repeating action potential; the second is the stimulus artifact, and the third is the driven motor unit complex.

2). Occasionally the firing of such a unit could be followed undisturbed in its regular, slow repetition during the recording, from an adjacent unit, of a high-frequency burst such as described above in Observation 4. (Note the lowest trace in Figure 3.)

6. Blocking of the motor nerve to a muscle in which spontaneous activity was being recorded in no case caused a change in this activity. Spontaneous volleys of action potentials continued to occur with equal frequency and with the same characteristics as those described in Observation 4. Likewise, slowly repeating, single-action potentials of the fibrillary type, as described in Observation 5, were found to continue undisturbed during and after nerve block (Figs. 3 and 4).

In no case did any of the control mice exhibit the above findings.

Although gross evidence of weakness and atrophy of involved muscles was characteristic of all seven dystrophic patients, four of the five who clinically were not of the myotonic type failed to exhibit the voluntary or spontaneous activity described in Observations 2, 3, and 4 above. One patient (Patient 3) showed no gross evidence of myotonia. His electrical record, however, included high-frequency bursts of action potentials, as described in Observations 3 and 4. We have refrained from classifying this patient as typically myotonic.

In two of the five nonmyotonic patients (Patients 3 and 6) the fibrillary type of action potentials, as described in Observation 5, was observed. In one patient (Patient 6) there was gross fasciculation which did not disappear under anesthesia, although electrical activity at that time was at a minimum. Slowly repeating single complexes were then observed to be completely asynchronous with the movements of fasciculation. In three of the five nonmyotonic patients no evidence of fibrillation was obtained.

Observations on the seven dystrophic patients are summarized in the Table.

Comment

One of the striking features which distinguishes dystrophia myotonica from other forms of dystrophy is the difficulty of re-

Observations on Seven Dystrophic Patients

Patient	Clinical Myotonia	E. M. G. Myotonia *	Fasciculation	Fibrillation
1	+	+	—	+
2	+	+	—	+
3	—	+	—	+
4	—	—	—	—
5	—	—	—	—
6	—	—	+	+
7	—	—	—	—

* Presence of "dive-bomber" bursts of action potentials.

laxation following vigorous use of muscle. Other features which are considered of diagnostic value in identifying this form of dystrophy include the peripheral distribution of the weakness and atrophy, and also the common findings of familial incidence, testicular atrophy, and cataract.[2,3] The "dive-bomber" bursts which characterize the electromyogram of such patients, and which have been considered the direct evidence of the peripheral myotonic reaction, have been found, however, in several forms of dystrophy and other myopathies, as well as in cases of peripheral nerve lesion and neuropathic atrophies.[4]

Several investigators have called attention to features which are common to both denervated muscles and the myotonic muscles of men and goats. Ravin[5,6] pointed out similarities in mechanical excitability, response to galvanic current, sensitivity to acetylcholine and potassium chloride, prolongation of early contractions, and the effects of epinephrine, quinine, and calcium in decreasing prolongation of contraction. Hypersensitivity to potassium chloride had been demonstrated by Brown and Harvey[7] in myotonic goats. These authors were unable to demonstrate, however, that sensitivity to acetylcholine in these animals was greater than in the normal. They also observed that myotonia in the goat becomes noticeably severe at a time following denervation which corresponds to the first appearance of fibrillation.

In attempting to distinguish between the peripheral myotonic response and what they chose to call the "after-spasm" of clinical myotonia, Denny-Brown and Nevin[8] demonstrated that the former is associated with "small rapid frequent action currents" and called attention to the fact that they "are exactly similar to those of muscle in fibrillation following denervation." Landau[9,10] reported that myotonic and fibrillation potentials, recorded with a small pick-up, are strikingly similar in the duration and voltage of individual complexes. He also demonstrated spontaneous synchronized activity in both denervated and myotonic muscle. Furthermore, the responses of the two to polarization were shown to be essentially the same. We have confirmed his observation that cathodal polarization increases fibrillary activity of denervated muscle.

In spite of the fact that many have recognized several features common to both myotonic and denervated muscle and that many have shown the phenomenon of peripheral myotonia to continue after nerve section or block,[7-9,11] no one suggests that myotonic dystrophy is due to denervation. In fact, it is generally accepted that neuron involvement is characteristic of neuropathies, but entirely fortuitous in myopathies. Adie and Greenfield[12] described "fibrillation" as prominent in a patient with dystrophia myotonica, but it is quite evident, however, that they referred to visible fasciculation in hamstring muscles of this patient. They recognized that their string galvanometer was not sufficiently sensitive to record either the myotonic or the "after-discharge" potentials during prolonged relaxation. The term fibrillation at this time was commonly used to describe fasciculation, a distinction not established until more sensitive recording instruments became available. Sargent[13] described a patient with peroneal muscular atrophy with myotonia in which he found "spontaneous fibrillation potentials at rest in all but the peronei and trains of high-frequency oscillation ('dive-bomber' sounds) in all muscles tested." This is a syndrome, however, in which pathological changes have been demonstrated in peripheral nerves and nerve roots.[14] Therefore the findings of fibrillation in this case can be accounted for on the basis of neuron destruction, resulting in actual muscle denervation. Shea, Woods, and Trator[15] and Walton[16] made a particular point of the fact that they were unable to find fibrillation associated with myotonia.

Our observations are fully in accord with the finding of a shift toward complexes of short duration in dystrophia myotonica, as stressed by Denny-Brown and Nevin,[8] Landau,[9] Walton,[16] and others. We are inclined to interpret as true fibrillation those

very short complexes (0.8-1.8 msec.) which repeat slowly (less than 15 per sec.) at very regular intervals over periods of many minutes and which are undisturbed by nerve block. Any change in rate of repetition is typically gradual rather than abrupt. These *are* the criteria by which fibrillation may be identified. Such potentials are not a prominent feature of the electromyogram in this disease, and often considerable search is required for their demonstration. We feel it important, however, to recognize that the finding of fibrillation is not inconsistent with a diagnosis of peripheral myopathy. Also it appears to be even more important that the recognition of the full gamut of spontaneous activity in the myotonic forms of dystrophy may help to elucidate mechanisms at the cell level in this disease.

The complete correspondence of the electromyographic findings in the Bar Harbor strain of dystrophic mice with those in patients with dystrophia myotonica suggests that these animals may be particularly valuable in the further study of this form of muscular dystrophy.

Summary

Electromyographic studies were made on 20 dystrophic mice of the Bar Harbor strain and on 7 dystrophic patients.

The findings in the dystrophic mice were the same as those in two cases of dystrophia myotonica and one case of progressive muscular dystrophy which exhibited electromyographic myotonia. These findings included weakness and atrophy, hyperirritability to mechanical stimulation, spontaneous high-frequency volleys, and fibrillation. Both the high-frequency volleys and fibrillary potentials continued undisturbed following nerve block in man and mouse.

Two of five dystrophic but nonmyotonic patients exhibited fibrillation.

It is concluded that the dystrophy of the Bar Harbor strain of mice corresponds closely to clinical dystrophia myotonica.

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Intracranial Aneurysms

Methods of Treatment; Value of Hypothermia in the Surgical Approach

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The proper management of intracranial arterial aneurysms has been the object of considerable controversy. In an effort to evaluate various methods of treatment, we have compared the results of these methods in 115 patients treated under similar conditions by the same surgeons. Before the evolution of modern neurosurgical techniques, intracranial aneurysms were curiosities, usually discovered at autopsy. In 1923 Symonds'[1] presentation of the criteria for the diagnosis of a ruptured intracranial aneurysm gave impetus to further study of this subject. Richardson and Hyland,[2] Walsh and King,[3] Dandy,[4] and numerous others have contributed much to the increasing frequency of diagnosis and successful treatment of aneurysms. Recently a more complete study by Hamby[5] has brought the entire subject into focus with a survey of the previous publications and an analysis of his own material.

The mortality rate of ruptured intracranial aneurysms is known to be high, ranging between 30% and 50% with the initial rupture and between 70% and 80% with recurrent rupture. Various types of treatment have been advocated, but the best method of management of patients with intracranial aneurysms, either ruptured or intact, has remained unsettled.

In general, the treatment of ruptured intracranial aneurysms by cervical carotid ligation has been the time-accepted method. It has been known to have a definite mortality and an even higher morbidity, but the excellent results which have been published concerning this method of treatment during the past 50 years are not to be disregarded. Nevertheless, carotid ligation is not a definitive and discrete procedure which precludes further rupture, since it simply reduces the force against an aneurysm. In addition, aneurysms on the middle cerebral artery in the Sylvian fissure and those on the anterior cerebral and anterior communicating arteries are less likely to be treated satisfactorily by carotid ligation. Consequently, many surgeons in the past have treated aneurysms about the circle of Willis by cervical carotid ligation, but have treated the aneurysms on the peripheral branches by intracranial approach. The direct approach has carried with it a high mortality, since the rupture of an intracranial vessel during operation frequently has made control of the bleeding aneurysm a difficult process, which, if not fatal to the patient, often results in hemiplegia.

With the advent of autonomic blocking agents to reduce the blood pressure during the surgical procedure, a safer intracranial approach seemed possible. The publication of Norlén and Olivecrona[6] gave added stimulus to this method. However, in most hands an intracranial approach, even with hypotension, carried a high mortality, and many surgeons preferred cervical ligation to the risk of an intracranial approach.

Although certain dramatic and gratifying results were obtained with each of the previous methods of treating intracranial aneurysms, there seemed to be no method that was consistently satisfactory and reasonably

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safe. To paraphrase Hamby,[5] "He [the neurosurgeon] was much in the position of the hunter arousing a tiger when stalking a deer," while, in reality, the neurosurgeon was seeking a method by which he could arouse a deer when stalking a tiger. In short, the desired end was a relatively simple method which could be safely applied to most patients with intracranial aneurysms.

Hypothermia, originally used in open surgical procedures and subsequently employed in intracranial operations, began to offer definite hope for a successful intracranial approach to aneurysms. By lowering cerebral metabolism and oxygen consumption, hypothermia permits temporary occlusion of cerebral blood flow without damage. This occlusion of blood flow provides a clean surgical field for the discrete and satisfactory ligation of the aneurysm.

Lougheed and Kahn[7] reported a 50% reduction in cerebral metabolism of dogs at a temperature of 30.0 C (86.0 F). Rosomoff and Holaday[8] reported a 50% reduction in cerebral oxygen consumption in dogs at 28.0 C (84.4 F). Botterell and others[9] pointed out that this reduction in cerebral metabolism permits a normal brain to tolerate interruption of circulation for approximately six minutes at 30.0 C. Obviously, the duration of safe interruption of cerebral circulation is influenced by the patient's age and the integrity of the cerebral blood vessels. Reduction of temperature below 30.0 C increases the danger of cardiac irregularities and does not significantly prolong the safe period of complete occlusion of cerebral circulation. It has been found, therefore, that a minimal temperature of 30.0 to 31.5 C (86.0 to 88.7 F) is desirable. This temperature range permits complete occlusion of the cerebral circulation by constriction of both common carotid and both vertebral arteries for a period of time which is both safe for the brain and, in most cases, adequate for the surgeon to effect the ligation of the aneurysm.

Clinical Data

The results in the treatment of 115 patients with intracranial aneurysms are presented. This series of patients, accumulated over the past nine years, includes the following categories: (1) those not treated by surgery; (2) those treated by cervical carotid ligation; (3) those treated by intracranial surgery without hypotension or hypothermia; (4) those treated by intracranial surgery with systemic hypotension; (5) those treated by intracranial surgery with hypothermia.

Although the number of patients in each category is too small to be statistically significant, the results obtained by each of the various methods do reflect the progress made in the treatment of intracranial aneurysms over the past 10 years.

The results of treatment are graded as excellent, good, fair, poor, or of fatal outcome. An excellent result is one in which there is no residual neurologic deficit, or only minimal pretreatment deficit which does not interfere with the patient's normal life and function. A good result indicates slight residual pre- or post-treatment deficit. A fair result indicates moderate residual pre- or post-treatment deficit which partially interferes with normal life. A poor result indicates severe residual pre- or post-treatment deficit which incapacitates the patient or seriously interferes with normal life.

All survival times in patients still living are based on follow-up examinations within the past three months, except for four patients who could not be located.

Patients Not Treated by Surgery.—Twenty-five patients admitted to the hospital with ruptured intracranial aneurysms were not treated surgically. Of these 25 patients, 14 died in the hospital. Seven of the fourteen who died in the hospital were so deeply comatose on admission that they could tolerate nothing more than supportive therapy, and they died within 26 hours after admission. The other seven patients who died in the hospital improved on conserva-

tive management, but before definitive studies could be carried out had a recurrent hemorrhage and died. Two of these seven patients became worse after carotid angiography.

Eleven patients with intracranial aneurysms verified by angiography were discharged from the hospital without surgical intervention. Operation was not performed because of multiple aneurysms, in five cases; medical contraindications, in three cases, and the patient's preference in three cases.

One patient with multiple aneurysms died of recurrent hemorrhage two months after discharge. Of the 10 patients who survived without surgery, 4 made an excellent recovery, 4 a good recovery, 1 a fair recovery, and 1 a poor recovery. Nine of these patients had only one hemorrhage. Seven of the nine now have survived three months to two years; two patients could not be located for follow-up. The 10th surviving patient had three hemorrhages within 6 weeks and now has lived 14 years since the last hemorrhage.

The desirability of deferring surgical intervention until the patient's condition stabilizes after hemorrhage must be weighed against the danger of recurrent hemorrhage during the period of delay. Of 115 patients in this series, 55 had more than one hemorrhage, 12 of these had three hemorrhages, 1 had four hemorrhages, and 2 had five hemorrhages. In three-fourths of the 55 patients with multiple hemorrhages the second hemorrhage followed the first one within 42 days, with an average interval of 15 days. In the remaining one-fourth the interval between the first and the second hemorrhage ranged from 6 weeks to 5 years, except for one patient, whose second hemorrhage occurred 15 years after the first one.

Patients Treated by Cervical Carotid Ligation.—In 33 patients treatment was by carotid ligation—27 with conventional methods of ligating, either the common or the internal carotid artery, and 6 with the method of gradual occlusion by means of the Selverstone clamp. In this group 10 died within 18 days after the ligation. In 4 of these 10, ligation was performed as an emergency procedure on a comatose patient for whom little hope was held for recovery.

One patient with an arteriovenous aneurysm of the internal carotid artery died at home of recurrent hemorrhage one month after carotid ligation. This aneurysm, 2.5 cm. in diameter, originated from the upper portion of the carotid siphon and communicated with the cavernous sinus. In various stages, the patient's common, internal, and external carotid arteries were ligated cervically, and finally the internal carotid artery was ligated intracranially distal to the aneurysm. Two other patients died of recurrent hemorrhage of the aneurysm—one four years after ligation of the carotid artery for an aneurysm of the anterior communicating artery and the other two years after ligation of the carotid artery for an aneurysm of the internal carotid vessel.

Of the 20 surviving patients, 15 had excellent results, 2 good results, 1 a fair result, and 2 poor results. Nineteen patients now have survived four months to eight years without recurrent hemorrhage; one patient could not be located for follow-up.

The results with the use of the Selverstone clamp were not as good as those with the conventional method of ligating the carotid artery. However, the patients selected for the Selverstone clamp were those who could not withstand sudden, complete carotid occlusion, but might tolerate gradual occlusion. Probably gradual occlusion with the clamp was not extended over a long enough period of time to prevent complications.

Patients Treated by Intracranial Surgery Without Hypotension or Hypothermia.—In 12 patients an aneurysm was treated by direct intracranial surgery without the use of hypotension or hypothermia. In all 12 patients the aneurysm had bled one or more times prior to surgery. Six patients died postoperatively. In four of these patients who died a direct intracranial approach

was undertaken as a desperate measure in a patient who was rapidly deteriorating and for whom the prognosis was poor. The other two patients, whose condition was good preoperatively, died as the result of complications of the direct surgical approach.

Of the six surviving patients, who now have survived from four to seven years, three had excellent results, two had good results, and one a poor result.

Patients Treated by Intracranial Surgery with Systemic Hypotension.—Because of dissatisfaction with the over-all results of the intracranial approach, systemic hypotension, produced by hexamethonium bromide, total spinal anesthesia, or, later, trimethaphan (Arfonad) was tried. In 15 patients the aneurysm was treated by intracranial surgery under systemic hypotension. Hypotension was induced with spinal procaine in 2 patients, with intravenous hexamethonium in 2 patients, and with intravenous trimethaphan in 10 patients. In one patient the administration of both trimethaphan and hexamethonium failed to reduce the blood pressure.

Seven patients died in the immediate postoperative period. One of these deaths was attributable to postoperative anuria with uremia, jaundice, and hyperkalemia.

Of the eight surviving patients, three had excellent results, two good results, one a fair result, and two poor results. Seven of these patients now have survived two to five years; one patient could not be located for follow-up.

While the intracranial approach in these cases was somewhat easier than in those without reduction of blood pressure, the operative field was still obscured by bleeding. The use of hypotension in the direct approach to aneurysms yielded no more satisfactory results than those obtained without hypotension.

Patients Treated by Intracranial Surgery with Hypothermia.—In the past two years 30 patients were treated by an intracranial surgical approach to an aneurysm under hypothermia. During this time four additional patients were treated by carotid ligation, for various reasons. Once the diagnosis of ruptured aneurysm was made, the earliest favorable time for surgical intervention was sought. Surgery was usually deferred until the patient had recovered from coma, the cerebrospinal fluid had begun to clear, and the intracranial pressure had become normal—usually within 5 to 14 days after the last hemorrhage. Assessment of the cardiovascular status and evaluation by the anesthesiologist were carried out in all patients.

In some of the earlier patients chlorpromazine and meperidine were given both at 10 hours and at 1 hour before operation. More recently the patients received chlorpromazine, 50 mg.; promethazine, 50 mg.; meperidine, 50 mg., and scopolamine, 0.2 mg., intramuscularly only at one hour before operation. After induction of anesthesia with intravenous thiopental (Pentothal) sodium, an endotracheal tube was inserted and anesthesia was maintained with nitrous oxide, or ether, or both. Promethazine was given by continuous intravenous drip to prevent shivering.

The anesthetized patient was placed in a canvas tub with chipped ice beneath and over him. His temperature, electroencephalogram, and electrocardiogram were recorded continuously throughout the entire procedure. The patient's temperature was measured in the earlier cases with a rectal thermocouple only, but in more recent cases, with both a rectal and an esophageal thermocouple. During the cooling process both carotid and both vertebral arteries were isolated by cervical dissection and tapes placed around them. When the temperature reached 31.4 C (88.5 F), usually after about two hours, the patient was removed from the tub of ice and placed on the operating table and the craniotomy was begun. After the patient's removal from the ice the temperature continued to drop, usually to about 30.0 C. Generally, at this temperature very little anesthesia was necessary during the actual operative procedure.

In the early cases, if bleeding occurred from the intracranial aneurysm after its exposure, an assistant, already in place beneath the surgical drapes, occluded the circulation completely by pulling on the tapes previously placed around the carotid and vertebral arteries. In a few recent cases the circulation was occluded for brief intervals, less than three minutes, even in the absence of bleeding from the aneurysm. This was done in order to reduce the tension in the aneurysm and, thereby, to facilitate clipping of the sac or its neck. The anesthetist recorded the time during which occlusion was maintained and informed the surgeons as each minute of time passed. Although occlusion of all four cervical arteries was maintained for as long as 12 minutes in one patient, who died postoperatively, usually it was not maintained for longer than 3 to 6 minutes, with an average of 4.4 minutes.

After the wound was closed and the patient's condition appeared to be stabilized, the patient was removed to the recovery room. If the patient's temperature was below 33.0 C (91.4 F), he was rewarmed with hot-water bottles and blankets until his temperature exceeded 33.0 C. More recently the patients were left on the operating table until the temperature reached 33.0 C or more.

The time required for the procedure, from induction of anesthesia to the closure of the surgical wound, averaged five hours, but in one case the entire procedure, including the cooling, the dissection of the neck, and the craniotomy, required only three and one-half hours.

Bleeding from scalp, bone, and dura mater was usually about the same as that encountered in an average craniotomy. The degree of relaxation of the brain obtained under hypothermic anesthesia did not differ significantly from that obtained under conventional anesthesia. Satisfactory retraction of the brain and exposure of the aneurysm were facilitated by cerebrospinal fluid drainage.

The ability to control safely any bleeding from the aneurysm by occlusion of the cervical vessels, thereby permitting discrete dissection and adequate obliteration of the aneurysm, has placed the field of intracranial surgery for aneurysms on a par with the previously highly developed field of intracranial surgery for tumors. On occasion, when occlusion of the cervical vessels for six to eight minutes did not provide sufficient time to dissect the neck of the aneurysm, the bleeding from the aneurysm was controlled by packing or by holding the aperture with a bayonet forceps, and the cervical vessels were released. The circulation thus was allowed to pass back through the brain for several minutes, and then a second period of carotid and vertebral arterial occlusion was effected.

At times the Mayfield spring clip was useful. This clip can be placed easily on the necessary intracranial artery, or arteries, to occlude circulation locally while the aneurysm distal to the occlusion is dissected. This delicate spring clip can be removed readily, without apparent damage to the vessel. Such a clip was also used in many instances on the neck of an aneurysm, or occasionally across the dome of an aneurysm, to occlude it. If such occlusion was satisfactory, the Mayfield clip was left in place, and the need for replacement with Cushing or Olivecrona clips was eliminated.

Postoperatively the temperature of most patients returned to normal within three to four hours, and the patient recovered consciousness much as in any other craniotomy with conventional anesthesia. In most instances the patient's postoperative course was smooth and uncomplicated.

In 30 patients in whom hypothermia was used there were 5 deaths. Among the 25 surviving patients there were 14 excellent results, 5 good results, 4 fair results, and 2 poor results.

Postoperative complications included four infected wounds, which healed after removal of the bone flaps. A third patient had nitrogen retention with electrolyte imbalance, and thrombophlebitis, from which

she recovered. A fourth patient had a partial third nerve paralysis, which gradually improved. A fifth patient had a mild Horner syndrome, and a sixth patient had a right-sided hemiparesis with personality changes, which improved.

In one of the five patients who died, ventricular fibrillation developed as he was being moved from the operating table, and he failed to respond, in spite of the use of all available methods of restoring normal cardiac rhythm. Because of technical difficulties his temperature had dropped to 25.0 C (77 F).

A second patient, with multiple aneurysms, had had the right internal carotid artery ligated in the neck two years earlier. He subsequently had hemorrhage from an aneurysm of the left internal carotid artery. Technical difficulties because of adhesions around the artery necessitated ligation of the left internal carotid artery intracranially, which resulted in death postoperatively.

A third patient had severely increased intracranial pressure postoperatively. She had had three episodes of intracranial hemorrhage in the 10 days prior to operation. Immediately before operation she had responded normally and had had a normal intracranial pressure. A fourth patient had markedly increased intracranial pressure with edema postoperatively. Autopsy revealed pulmonary edema, atelectasis, and occlusion of the right main-stem bronchus with mucus. A fifth patient responded well for 2 days, but showed cardiac decompensation and pneumonia on the 3d day and died on her 10th postoperative day.

There was one other cardiac complication in a patient who had two episodes of atrial fibrillation, while her temperature was 28.5 C (83.3 F). The arrhythmia cleared, and she had no other difficulties after she was rewarmed to her normal temperature.

An effort has been made to correlate the duration and extent of carotid and vertebral arterial occlusion with the postoperative result. Table 1 lists the temperature and duration of vascular occlusion for each patient. All five patients who died had both carotid and both vertebral arteries occluded from 1½ to 12 minutes. However, there were five patients with excellent results in whom the carotid and vertebral arteries were occluded for as long as 1 to 4 minutes, and one patient with an excellent result had the internal carotid artery occluded intracranially for 12 to 14 minutes. In 15 patients occlusion of the cervical arteries was not utilized, but it should be emphasized that this method of control was available in all cases. Hemorrhage from the

TABLE 1.—*Vascular Occlusion with Hypothermia*

Patient	Age	Minimum Temp. C	Duration of Occlusion of Cervical Vessels,* Min.	Occlusion of Other Vessels	Results of Treatment
1	49	25.0	2-3	Mid. cer. — 3 min.	Died
2	35	29.6	11; 12	0	Died
3	42	30.0	5	0	Died
4	37	29.5	5⅚	0	Died
5	56	30.4	1½	0	Died
6	35	30.6	1	0	Excellent
7	17	29.0	0	0	Excellent
8	33	27.8	0	0	Excellent
9	44	30.6	0	0	Excellent
10	51	30.0	1	0	Excellent
11	41	30.3	0	Int. car. † — 5 min.	Excellent
12	28	29.2	0	0	Excellent
13	30	31.5	3-4	0	Excellent
14	47	28.0	1; 4	0	Excellent
15	36	30.1	0	Int. car. † — 12-14 min.	Excellent
16	43	28.5	0	0	Excellent
17	25	30.0	0	Mid. cer. — 4 min.	Excellent
18	43	29.0	0	Mid. cer. — 6½ min.	Excellent
19	36	28.5	3½	Mid. cer. — 5 min.	Excellent
20	32	31.0	8	Mid. cer. 16 min.	Good
21	35	28.6	0	0	Good
22	65	26.8	4½	0	Good
23	52	30.8	9	Ant. cer. — 10-11 min.	Good
24	44	30.4	0	0	Good
25	39	31.5	0	0	Fair
26	54	29.8	0	0	Fair
27	23	30.0	0	Left ant. cer., 18 min; later both ant. cer., 4 min.	Fair
28	54	30.7	2½ ‡	0	Fair
29	66	30.4	8-9	Ant. cer. — 12 min.	Poor
30	59	31.0	0	0	Poor

* Both carotid and both vertebral arteries.
† Intracranial portion.
‡ Left vertebral artery could not be isolated.

TABLE 2.—*Summary of Results*

Method of Treatment	Total No.	Died	Excellent	Good	Fair	Poor
No surgery	25	15 (60%)	4 (16%)	4 (16%)	1 (4%)	1 (4%)
Carotid occlusion						
Ligation	27	7 (26%)	14 (52%)	2 (7%)	2 (7%)	2 (7%)
Selverstone clamp	6	3 (50%)	2 (33%)	0	0	1 (17%)
Total	33	10 (30%)	16 (48%)	2 (6%)	2 (6%)	3 (9%)
Direct — unmodified	12	6 (50%)	3 (25%)	2 (17%)	0	1 (8%)
Direct — hypotension	15	7 (47%)	3 (20%)	2 (13%)	1 (7%)	2 (13%)
Direct — hypothermia	30	5 (17%)	14 (47%)	5 (17%)	4 (13%)	2 (6%)
All surgery	90	28 (31%)	36 (40%)	11 (12%)	7 (8%)	8 (9%)
All patients	115	43 (37%)	40 (35%)	15 (13%)	8 (7%)	9 (8%)

aneurysm could have led to disaster, but for this quick and safe temporary control of bleeding until the aneurysm could be discretely clipped.

Comment

Comparison of Results of All Methods of Treatment.—In order to compare the results of the various methods of treatment a summary of the results of each method is presented in Table 2. As emphasized earlier, the number of patients in each category is too small to be statistically significant. The percentage figures in Table 2 are valuable as an indication of our experience with the various methods.

The figures presented in Table 2 include all results, regardless of the patient's preoperative condition. In evaluating the mortality for each method, we have reaffirmed the important prognostic value of the pretreatment status. Of the patients who died, there were several in each group who were in such critical condition prior to treatment that they probably would not have done well with any method of treatment. Elimination of those patients yields the following comparison of mortality rates of the various methods of treatment:

	Per Cent
No surgery	44
Carotid occlusion	21
Intracranial surgery, unmodified	25
Intracranial surgery with hypotension	43
Intracranial surgery with hypothermia	11

The pretreatment condition of the patient was an important prognostic factor in the results in the patients who survived. The correlation between the state of consciousness on admission and the patient's general status was reliable, and the prognosis was considered to be much worse when the patient was comatose. Usually patients with hemiplegia or hemiparesis had poorer results than those patients without such pretreatment deficit. Cranial nerve palsies were not indicative of an impending poor result.

Of the patients who were not treated surgically, only those in good or in fairly good condition on admission made an excellent or a good recovery. However, among the patients treated surgically there were several—especially in the group treated under hypothermia—who were in poor or fair preoperative condition but who made an excellent or good recovery.

The question might well be raised as to whether the improved results in patients treated under hypothermia are due to increased experience on the part of the surgeons. However, the intracranial approach with hypotension was undertaken at a later period than the unmodified intracranial approach and yielded no better results; therefore, it would seem that the improvement of results with hypothermia cannot be credited solely to experience.

Evaluation of Results of Treatment According to Location of Aneurysm by All Methods of Surgery.—A summary of the results of treatment of aneurysms according to their location is presented in Table 3 to permit comparison with other published

TABLE 3.—*Summary of Results According to Site of Aneurysm*

Site of Aneurysm	Total No.	No Surgery	Carotid Occlusion	Intracranial, Unmodified	Intracranial, Hypotension	Intracranial, Hypothermia	Summary Surgical Results
Int. car.-post. comm. junction	36	Died 4 Good 1 Poor 1	Died 7 Excell.* 9 Good 2 Fair 1 Poor 1	0	0	Died 1 Excell. 7 Good 1 Poor 1	Died 27% Excell.-good 63% Fair-poor 10%
Int. car. (not at post. comm. junc.)	29	Died 3 Excell. 2 Good 1	Died 3 Excell. 5 Fair 1† Poor 1†	Died 1 Excell. 1 Good 1 Poor 1	Excell. 1 Good 1	Died 2 Excell. 3 Fair 2	Died 26% Excell.-good 52% Fair-poor 22%
Ant. comm.	21	Died 2 Fair 1 Poor 1	Excell. 1†	Died 2 Good 1	Died 4 Fair 1 Poor 1	Died 1 Excell. 1 Good 2 Fair 2 Poor 1	Died 41% Excell.-good 29% Fair-good 29%
Ant. cer.	11	Died 1 Excell. 1 Good 1	0	Died 2 Excell. 1	Died 2 Excell. 1 Good 1	Good 1	Died 50% Excell.-good 50%
Mid. cer.	20	Died 4 Excell. 1 Good 2	Excell. 1 Poor 1	Died 1 Excell. 1	Died 1 Excell. 1 Poor 1	Died 1 Excell. 3 Good 1 Fair 1	Died 23% Excell.-good 54% Fair-poor 23%
Basilar	2	Died 2	0	0	0	0	No surgery

* Excellent.
† Patient had postoperative results, as indicated, but died later of recurrent hemorrhage (see text).

series. This may be summarized as follows:

Site of Aneurysm	Died, %	Excellent or Good Results, %
Junction of internal carotid and posterior communicating arteries	27	63
Internal carotid artery, distal or proximal to posterior communicating artery	26	52
Anterior communicating artery	41	29
Anterior cerebral artery	50	50
Middle cerebral artery	23	54

TABLE 4.—*Mortality and Results of Various Treatment Methods*

Method of Treatment	Total Mortality of All Patients, %	Mortality of Patients in Fair to Good Pretreatment Condition, %	Excellent or Good Results, %
No surgery	60	44	32
Carotid occlusion	30	21	54
Direct intracranial surgery, unmodified	50	25	42
Direct intracranial surgery with hypotension	47	43	33
Direct intracranial surgery with hypothermia	17	11	64

Summary

The results of the treatment of 115 patients with intracranial arterial aneurysms are presented. The mortality and the excellent or good results of the various methods of treatment are presented in Table 4.

Conclusions

Undoubtedly some previously ruptured intracranial aneurysms will not rupture again over long periods of time and will be accompanied by excellent results without surgery. It is impossible to predict such cases, and the mortality for nonsurgically treated cases is high—at least 60%.

The choice of operative procedure for those patients to be treated by surgery seems to rest between cervical ligation of the carotid artery and intracranial approach under hypothermia.

The mortality of cervical ligation of the carotid artery is relatively low, and many excellent results can be obtained by this method. This procedure does not obliterate the aneurysm and, therefore, has the disadvantage of leaving the patient liable to a

recurrent rupture at a later date. There were three ruptures after cervical carotid ligation in this series. In very large aneurysms or in patients for whom anesthesia and hypothermia are contraindicated, carotid ligation may be the method of choice.

The mortality of direct surgical approach under hypothermia can be kept as low as, or lower than, that of carotid ligation. In such circumstances the advantage of completely obliterating the aneurysm is a real one. Familiarity with this technique will give the surgeon a facility in the handling of intracranial aneurysms which will produce results superior to those of any other method now available. Although temporary, complete occlusion admittedly is not essential in the management of all patients, it being impossible to predict accurately who will require it, and it should, therefore, always be available.

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Production of Hydrocephalus by Increased Cephalic-Venous Pressure

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The relationship of increased cerebral venous pressure to ventricular enlargement and hydrocephalus has never been satisfactorily worked out. The interdependence of intracranial pressure and cerebral venous pressure has been recognized both in clinical problems and in experimental studies, but the possibility of cerebral venous pressure as a primary cause of ventricular enlargement has remained a controversial issue.

Dandy [2] stated that the occlusion of the vein of Galen would cause hydrocephalus. Others have tried this and other types of experimental venous occlusions, with varying results. Russell,[4] in her monograph on hydrocephalus, reviewed much of this work, including some experimental work of her own, and concluded that, while hydrocephalus had apparently been produced in some instances, the results were, in general, equivocal. These experimental attempts to produce hydrocephalus from increased venous pressure were all based upon local occlusion of a cerebral vein or dural sinus. This allowed the possibility that collateral circulation might have been sufficient to keep the venous pressure at normal levels, or that the venous occlusion produced only a local, and perhaps temporary, increase in venous pressure. If the entire cephalic venous drainage were occluded, the elevation of the cerebral venous pressure would be general and could be sustained for protracted periods. This paper presents the results of an investigation of this hypothesis in dogs. After blocking the major venous drainage routes from the head in the neck and spinal canal, the animals were observed over a period of time for the development of hydrocephalus.

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Materials and Methods

The experimental animals were 26 mongrel dogs, weighing about 20 kg. each: 21 for observations on the development of hydrocephalus and 5 for control studies. The occlusion of the cephalic venous drainage was accomplished by ligating and removing a segment of both the internal and the external jugular veins low in the neck proximal to the junction with the facial vein, and bilaterally occluding the condyloid foramen at the base of the skull. This procedure blocks the major venous drainage of the head and the major anastomotic channels to the spinal venous system (Worthman,[5,7]). One week following this procedure the neck dissection was carried out again, and any veins found were ligated and divided. At various intervals after the second ligation the animals were killed so that the brains could be examined for the development of hydrocephalus. The sagittal sinus venous pressure was measured by catheterizing the sinus in the midparietal region. The intracranial pressure was measured either through percutaneous cisternal puncture or ventricular tap through a

TABLE 1.—*Cerebrospinal Fluid Pressures and Superior Sagittal Sinus Venous Pressures in Normal Dogs and Dogs Made Hydrocephalic by Injection of Kaolin into the Cisterna Magna*

		No. Observ.	Mean Pressure Mm. H_2O	Range, Mm. H_2O
Normal dogs	CSFP	163	100±1.9	30-180
	SSVP	51	88±3.6	35-142
Dogs with kaolin produced hydrocephalus	Vent. pres.	119	165±6.4	55-400
	SSVP	63	120±7.3	20-315

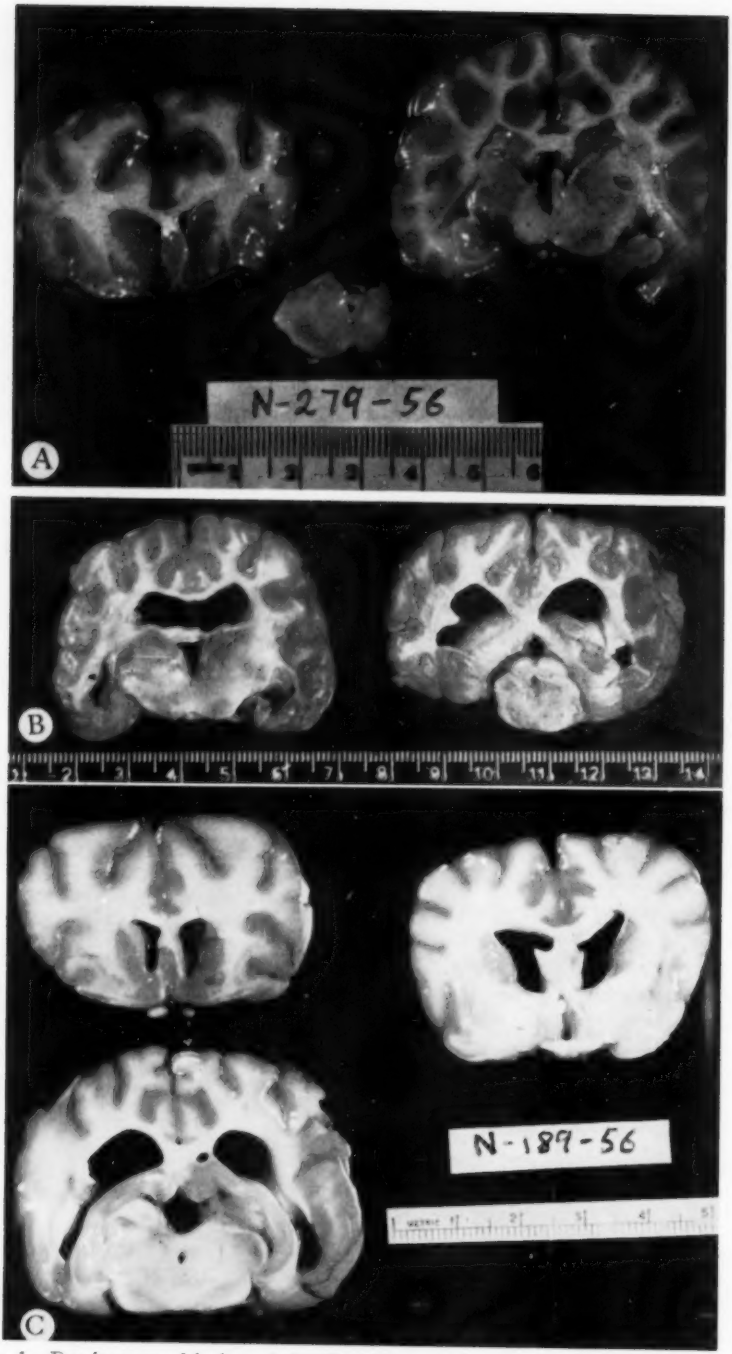

Fig. 1.—Development of hydrocephalus following cephalic venous occlusion. *A*, normal dog brain; *B*, two weeks after venous occlusion, showing enlarged ventricles and ruptured septum pellucidum; *C*, eight weeks after venous occlusion, showing about the same degree of hydrocephalus as at two weeks.

cranial burr hole. The venous circulation was studied by x-ray sinography. Some ventriculograms were made with iophendylate (Pantopaque) and some with air. Cerebrospinal fluid and sagittal-sinus pressure and pulsation tracings were made on a Statham strain gauge, recorded on a Sanborn Poly-Viso recorder. All pressures were measured with animals on their right side and the level of the right cardiac atrium taken as zero.

Results

Five dogs, designated as control studies, were used in developing the techniques of venous occlusion, measurements of sagittal sinus venous pressure (SSVP), cerebrospinal fluid pressure (CSFP), venous circulation by sinography, and measurement of ventricular size. Similar pressure data from other experiments in the laboratory were combined to get the normal pressure values and ranges. The CSF pressure ranged from 30 to 180 mm. H_2O, with a mean of 100 ± 1.9 mm. H_2O. The sagittal sinus venous pressure ranged from 35 to 192 mm. H_2O, with a mean of 88 ± 3.6 mm. H_2O. These values, along with data from hydrocephalic dogs (cisternal kaolin [1]) are shown in Table 1.

Sinography showed that the major venous drainage routes were occluded by the method described, confirming the observations of Worthman.[6,7] Thirteen, or 74% of the dogs, developed hydrocephalus as a result of the occlusion of the cephalic venous drainage, and eight, or 26%, did not. None of the dogs showed any clinical neurological deficit.

The 13 dogs which developed hydrocephalus were killed at intervals after the second ligation of 4, 6, 10, 12, 14, 17, 26, 31, 36, 52, 56, 67, and 68 days. Ventricular enlargement was the only gross change seen in the brains at autopsy. The ventricular enlargement was not continually progressive, but seemed to reach its peak about two to three weeks after the second neck dissection and then remain stabilized (Fig. 1). The degree of hydrocephalus was never as great as that seen following plugging of the aqueduct of Sylvius [3] or following cisternal injection of kaolin,[5] where the hydrocephalus seems to be steadily progressive. The septum pellucidum ruptured in 50% of the dogs with hydrocephalus following cephalic venous occlusion. This finding has not been commonly observed in animals with aqueduct occlusion or kaolin meningitis, but sufficient data are not available to state whether or not this represents a true difference.

Both the CSF pressure and the SSVP were elevated after the venous blockade. Initially the CSF pressure was greater than the SSVP, as is usual, but within a few days the CSF pressure had fallen below the SSVP and remained there. This was a reversal of the usual relationship between these two pressures. Both pressures fell with time, although normal levels were never reached in these experiments (Fig. 2). The maximum CSF pressures were seldom over 200 mm. H_2O, which is in the range of the mean CSF pressures seen in other types of hydrocephalus, but considerably below the maximum. The sagittal sinus venous pressure, however, was somewhat higher than is usually seen in other types of experimental hydrocephalus (Table 1 and Fig. 1).

The venous pressure fall was probably a reflection of the development and enlargement of the remaining venous collateral drainage, as shown by the sinographic stud-

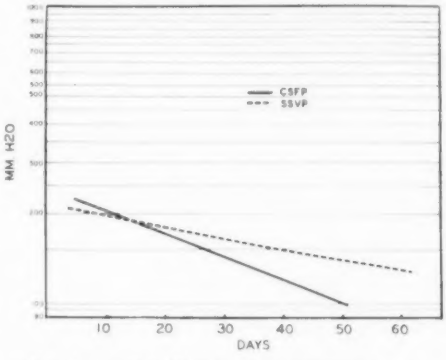

Fig. 2.—Cerebrospinal fluid pressures and superior sagittal sinus pressures in dogs following occlusion of the major cephalic venous drainage routes from the head. The lines represent the mean data from 21 experiments.

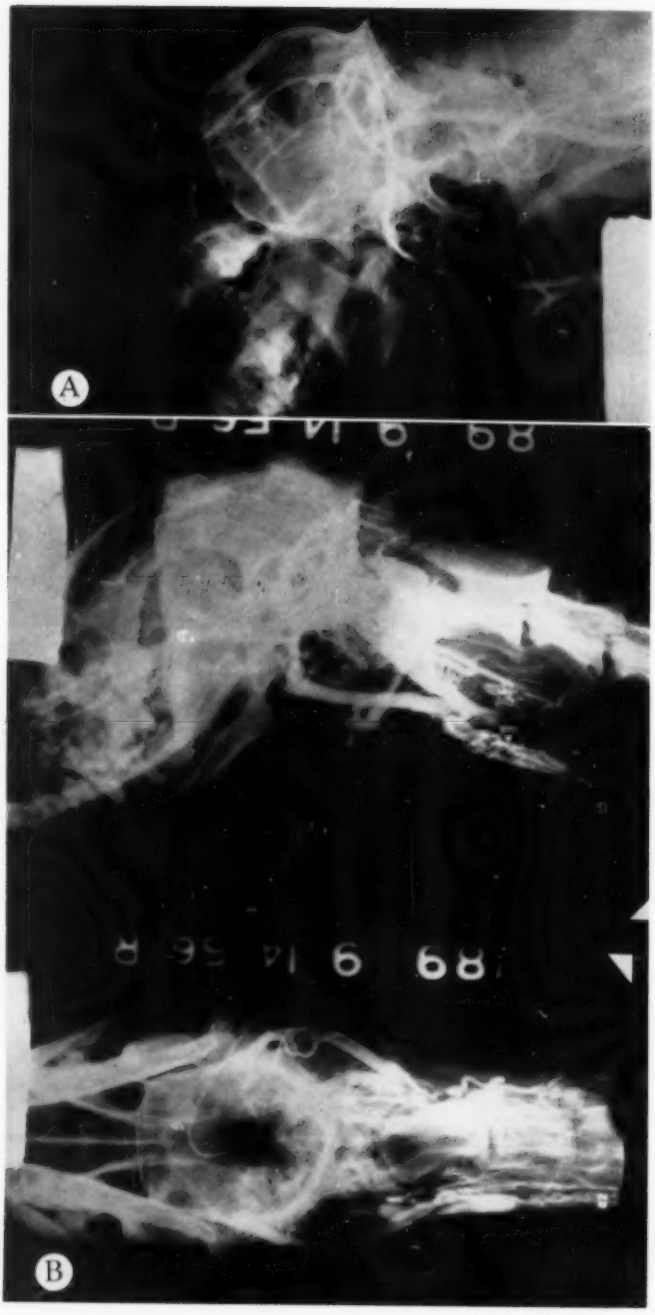

Fig. 3.—Sinograms and cephalic venograms before and after cephalic venous occlusion. *A*, oblique view of normal dog, showing major venous drainage routes through external jugular and condyloid veins. *B*, anteroposterior and oblique views 56 days after venous occlusion, showing development of collateral channels.

ies. Anastomotic channels developed around the jugular occlusions by enlargement of numerous small vessels in the neck. In some animals small vessels in the paravertebral muscles enlarged to reestablish a connection with the spinal venous system. Sinograms made on (*A*) a normal dog and (*B*) 57 days after cephalic venous occlusion are shown in Figure 3.

The normal dog tolerated iodopyracet (Diodrast) sinography very well, but this procedure was lethal in all instances in which it was done soon after the venous occlusion. Sufficient data were not obtained to relate this fact accurately to the level of cerebral venous pressure or other factors.

Eight animals did not develop hydrocephalus. One was killed the day his ligations were completed. Another was considered to have an incomplete ligation and therefore also was not expected to develop hydrocephalus. The remaining six were killed, one at 7 days, two at 14 days, and one each at 28, 37, and 46 days. All of these animals had significantly elevated CSF and SSVP pressures, so that the reason that hydrocephalus did not develop is not entirely clear.

Cerebrospinal fluid pulsation (cisterna magna) was measured in eight animals before and after occlusion of the cephalic venous drainage. Three of these dogs became hydrocephalic, and five did not. The CSF pulsation was found to be increased in all of the hydrocephalic dogs, but in only one of the dogs whose ventricles did not enlarge. The one dog which had an increased pulse without ventricular enlargement was different in that the pulse measurements were made 10 days after venous occlusion, although the animal was not killed and the ventricles examined until 28 days after occlusion. The other animals all had pulse pressure studies done at the time they were killed. The pulse data are shown in Table 2.

Comment

This work shows that ventricular enlargement can result from a chronic general increase in the cerebral venous pressure. It is important to reemphasize that these experiments differed from past work in that the intracranial cavity was not invaded, all local venous channels remaining open, nor was there any direct damage to the brain to complicate the picture. The subarachnoid pathways were all open, so that the hydrocephalus was truly communicating.

The mechanisms involved in the ventricular enlargement seemed to be a combination of at least two factors. One was the possible failure of CSF absorption in the face of increased SSVP pressure, and the other was the increased intraventricular pulse pressure from the choroid plexus.

The failure of absorption of CSF in the face of increased venous pressure is related to the pressure gradient between the CSF and the SSVP. This pressure difference is considered to be one of the major forces concerned with CSF absorption. In these

TABLE 2—*Cerebrospinal and Sagittal Sinus Pressure Data Before and After Occlusion of the Major Cephalic Venous Drainage of the Dog*

	Preocclusion				Duration After Venous Occlusion	Postocclusion				
	CSF		Sagittal Sinus			CSF		Sagittal Sinus		
Dog	Pressure	Pulse	Pressure	Pulse		Pressure	Pulse	Pressure	Pulse	Hydrocephalus
N-151-57	110	6	76	2.5	7	210	8	175	5	None
N-16-56	95	7	85	1	10	130	21			None
N-170-57	145	9	110	4	14	190	5	200	3.5	None
N-171-57	110	9	60	4	14	185	3	195	3	None
N-466-57	70	10	88	2	37	185	10	175	2	None
N-2-57	85	7	83	2	31	245	21	235	7	Moderate
N-129-57	90		76		52	195	19	220	6	Slight
N-481-57	90	6	87	2	68	180	35	185	4	Moderate

experiments the CSF pressure was initially increased and somewhat higher than the SSVP, but within a few days the CSF pressure fell below that of the venous pressure, an unusual and abnormal situation. If these pressure changes mean failure of CSF absorption, the development of hydrocephalus is understandable as a natural consequence. However, in the dog the CSF can escape through the cribriform plate into the lymphatic system.[5] This may account for the CSFP drop and the failure to develop hydrocephalus in some dogs.

Another explanation for the ventricular enlargement was the increased intraventricular pulse pressure.[1] This was the result of the distended and obstructed venous system, which could not exert its usual damping effect on the choroid plexus pulsation. Thus the interior of the brain was subjected to an increased pulsation pressure, which resulted in ventricular enlargement commensurate with the pulsation increase. While the amount of data on this subject is not large, it is important that in those animals where the pulse pressure was measured, it was elevated in the hydrocephalic animals and not elevated in three of the four animals which did not show ventricular enlargement. This mechanism would explain the limited ventricular enlargement without progression seen in these animals.

These experiments suggest the possibility that increased cerebral venous pressure could be the primary cause of communicating hydrocephalus. Such a patient has not yet been found, but only a few cases have been studied with this in mind. While the effects of increased venous pressure are only speculative as a primary cause of hydrocephalus, they certainly must have some secondary effects. The increased intracranial pressure from whatever cause raises the cerebral venous pressure, which, in turn, adds another increment to the intracranial pressure. This results in a vicious cycle, which is broken only by the successful reduction of the intracranial pressure.

Summary

The cephalic venous pressure of dogs was elevated by occluding all the major drainage routes in the neck and anastomoses with the spinal canal at the condyloid foramen.

This procedure resulted in hydrocephalus in 74% of 21 dogs. The hydrocephalus was not steadily progressive but reached a maximum in two to three weeks.

Both the sagittal sinus venous pressure and the cerebrospinal fluid pressure were initially elevated but slowly fell as time progressed, presumably because of the development of collateral venous drainage.

The role of the choroid plexus pulsation in the mechanism of the ventricular enlargement is discussed.

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Guillain-Barré Syndrome and Virus of Influenza A (Asian Strain)

Report of Two Fatal Cases During the 1957 Epidemic in Wales

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Although the major complication of the 1957 pandemic of influenza was pneumonia, cases of neurological disorder were reported to accompany or to follow the initial respiratory infection. The brunt of the insult was borne at any level of the nervous system, giving rise to a varying combination of clinical symptoms and signs. One of these was the Guillain-Barré syndrome.

Despite the occurrence of fatal cases and the opportunity for pathological study, this syndrome remains a clinical concept, although, since its first description in 1916,[16] the ambit of its diagnostic use has been greatly extended, particularly in the literature of Scandinavia, America, and the British Commonwealth. By the outbreak of World War II, Guillain[14] himself had accepted several varieties of the syndrome, and in his most recent communication[15] (1953) he allotted 3 of his series of 19 cases to a sixth variety, which had been described nearly 20 years earlier by Dubois and van Bogaert[8] (1936). Baker[1] (1943) classified his 33 cases in five groups, and Haymaker and Kernohan[18] (1949) distinguished seven separate clinical presentations in the large series which they discussed, including 50 cases of their own.

It is helpful, therefore, to recall the basic symptoms and signs which were described more than 40 years ago,[16] and which Guillain[15] has restated in his 1953 review. These are muscular weakness; loss of tendon, but not of superficial, reflexes; paresthesiae with slight sensory disturbance; tenderness of muscle on pressure; minor changes in the electrical reactions of muscle and nerve, and increase of protein in the cerebrospinal fluid without change in the number of cells. On the importance of this famous *dissociation albumino-cytologique* he remains adamant, appreciating that this may not be found at the first lumbar puncture, but stating categorically, that cases with a cell count of 100 to 150 lymphocytes per cubic millimeter in the spinal fluid cannot be included in the syndrome. His conservative approach to the widening of the clinical boundaries of the syndrome has been clearly stated.[15]

Dans la vaste synthèse de Webb Haymaker et James W. Kernohan, où sont englobées les maladies les plus différentes des nerfs, des racines, de la moelle épinière, du bulbe rachidien, synthèse dans laquelle les analyses chimiques et cytologiques du liquide céphalo-rachidien n'ont, d'après eux, aucune importance, je ne reconnais aucunement le syndrome que j'ai décrit avec J-A. Barré.

The morbid histological findings are variable and do not always accord with the clinical observations. The main changes, however, are found in the lower motor and primary sensory neurons, and this basic pathological lesion has been described as a polyneuronitis (Brain,[4] 1955). Their pathogenesis is imperfectly understood, although recent opinion suggests that a tissue sensitivity reaction is at least partly responsible. It should, therefore, be emphasized that much of this reasoning is based on analogy with the neurological

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syndromes following prophylactic inoculation (Miller and Stanton,[31] 1954) and with the results of experiments on animals (Waksman and Adams,[42] 1955). In view of the limitations of the histological method, a new angle of approach is welcome. The increasing range of virus antibody studies, together with the isolation of virus from body fluids and tissues in life and post mortem, offers such a method.

Since the first reports appeared in World War I, no single etiological agent has been identified, despite the early claim of Bradford, Bashford, and Wilson[3] (1918), but in recent years the syndrome has been recognized as a complication of specific infections, notably viral pneumonia (Holmes,[21] 1947; Jennings,[23] 1952) and infectious mononucleosis (Ricker et al.,[36] 1947; Peters et al.,[34] 1947). Guillain,[15] while acknowledging that the syndrome had been described as a sequel to many common exanthemata, to exposure to bis(2-chloroethyl) sulfides (mustard gas), smallpox vaccination, and Coxsackie viral infections, and, most frequently, to mononucleosis, hepatitis, and brucellosis, considered that a specific virus was the causal agent. Campbell[5] (1958), in a series of 11 cases, of which 6 had been observed personally, found that the onset of the disease in man followed closely on infection in cats with which the patients had been in contact. He gave reasons for supposing that the animal disease was feline enteritis. Casals[6] (1958) was unable to cite any proof of a viral etiology.

When Greenfield[13] (1930) described his two cases of encephalomyelitis following an influenza-like illness, he was careful to point out that there was no pathological confirmation of infection with influenza. At that time no virus of influenza had been isolated (Smith, Andrewes, and Laidlaw,[40] 1933). His report seemed to give new impetus to the clinical association of influenza with neurological disorders, although, in Great Britain, virological support in cases of the Guillain-Barré syndrome was not forthcoming until 1952; in that year Jennings recorded a titer of 1:16 to influenza A virus in a female patient aged 56 with severe polyneuritis.[23] In some reports, tests for known viruses had been carried out and were negative, but the search for these may not have been energetic. Haymaker and Kernohan[18] found that virus studies had been made in only 17 of the 50 fatal cases which they studied. Guillain,[15] in reporting 19 cases seen between 1936 and 1947, referred to 1 case only in which transfer of the suspected virus to experimental animals had been tried.

During the autumn of 1957 several cases occurred, in South Wales, of illness due to the Asian strain of influenza A virus which were complicated by neurological symptoms and signs. Four of these have already been reported by our colleagues (McConkey and Daws,[28] 1958); we have seen, or examined the serum of, nine others. The essential data of these nine cases are presented in the accompanying Table. Two of the patients who died presented with the Guillain-Barré syndrome and are considered in this report.

Report of Cases

Case 1.—This 53-year-old man was injured in the face on Sept. 14, 1957, and was found to have compound fractures of both rami of the mandible. On Sept. 18 open reduction of the fractures and stabilization by wiring were performed under general anesthesia. Postoperative progress was normal, and he was ambulant by the second day.

On Sept. 23 he complained of "pins and needles" sensation in his hands and feet; weakness of his legs developed during that day. Next morning he was unable to stand. During the next 72 hours his condition deteriorated, the limb weakness becoming more intense, and he was unable to sit up without help. He had no difficulty in passing urine, and this exception to the general loss of power continued to the end.

At 8 p.m. on Sept. 27 he was seen by one of us (C. E. C. W.). The patient was alert, orientated, and cooperative. Temperature 99.4 F; pulse 120 and of regular rhythm; B. P. 130/80. Respirations were shallow, and accessory muscles were in play. He could not count beyond 16 in a single breath. Rales were audible on auscultation of the larynx, but were readily cleared by aspiration. The bladder was not distended.

Cases of Neurological Disorder Occurring in South Wales at Time of Epidemic of Influenza A (Asian Strain), September-December, 1957

Case No.	Sex	Age	Clinical Diagnosis	C. S. F. Cells/ Cu. Mm.	C. S. F. Protein, Mg. %	Virus Investigations C. F.: Complement-Fixing Titer to Influenza A Virus
1	M	53	Guillain-Barré	<5	82	C. F.: 1/32 on 5th day of illness; Influenza A (Asian strain) virus isolated from lung tissue and from C. S. F. taken 6 hr. post mortem (death on 8th day of illness)
2	F	38	Guillain-Barré	Not examined		C. F.: 1/64 on 13th day of illness; Influenza A (Asian strain) virus isolated from C. S. F. taken 4 hr. post mortem (death on 13th day of illness)
3	F	59	Myelitis	440	180	Influenza A (Asian strain) virus isolated from brain and spinal cord at autopsy (death on 10th day of illness)
4	F	35	Encephalitis	40	26	C. F.: 1/32 on 8th day of illness <1/8 on 30th day of illness
5	F	43	Encephalitis	<5	15	C. F.: 1/1024 12th day of illness
6	M	47	Encephalitis	54	90	C. F.: 1/2048 15th day of illness
7	F	16	Encephalitis	Not examined		C. F.: >1/512 14th day of illness
8	M	10	Encephalitis	Not examined		C. F.: 1/128 10th day of illness 1/64 22nd day of illness
9	F	23	Myelitis	56	60	C. F.: 1/8 11th day of illness 1/32 18th day of illness 1/16 30th day of illness

The neurological examination revealed a profound motor weakness, involving all four limbs and the muscles of the trunk. No facial weakness was present at this stage. Neck movements were free and painless. The pupils were equal and their reactions normal. The ocular fundi were normal. Movements of the external ocular muscles were apparently full, although the patient stated, during this test, that he had seen double earlier in the day. Hearing was unimpaired, and the drums were healthy. Examination of the lower cranial nerves was necessarily limited by his injuries. Dysphagia was not observed when he was fed by pipette, and no fluid was regurgitated through his nose. Sensation to light touch and pinprick was normal over the face; the corneal reflexes were equal.

With the exception of the left biceps jerk, from which a flicker was elicted, the tendon reflexes were not obtained. Abdominal reflexes were absent. The plantar responses were inactive.

Light touch, pain, joint position, and vibration senses were examined. All four modalities were depressed at the periphery of limbs. The patient reported some alteration in the quality of pinprick at the root of the neck, but no clear-cut sensory level could be demonstrated. Light touch was appreciated normally over the trunk and proximal segments of the limbs, but vibration sense was impaired. The sensation of pain was preserved in the saddle area. The muscles of the calf and thigh were tender on deep pressure.

After his transfer to Cardiff Royal Infirmary, under the care of Dr. J. D. Spillane, tracheostomy was performed under local anesthesia, and respiration was assisted with an automatic apparatus. During the succeeding days his neurological status remained unchanged except for the appearance of bilateral facial paresis. At 7:50 a. m. on Oct. 1, 1957, he lost consciousness suddenly and died.

Shortly after admission to Cardiff a lumbar puncture was performed. The fluid was clear and under a pressure of 110 mm. of water. It contained less than 5 leukocytes per cubic millimeter, 82 mg. of protein and 98 mg. of sugar, per 100 ml. Bacterial culture was sterile.

Blood count showed hemoglobin 13.6 gm. per 100 ml., and white cells 20,300 per cubic millimeter (91% polymorphonuclears, 2% metamyelocytes, and 7% lymphocytes). The red cells appeared normal on the films. Serum electrolytes were estimated as follows: sodium 135 mEq.; potassium 4.2 mEq., and chloride 98 mEq., per liter. No urinary porphyrins were found.

Pathology.—Autopsy, three hours after death, showed acute inflammation of the trachea and small bronchi, but otherwise the gross appearance of the viscera was normal.

An unruptured berry aneurysm, 7 mm. across, was present on the intracranial part of the left vertebral artery. The vessel was patent. There was also an excess of cerebrospinal fluid. Otherwise the nervous system was normal to the naked eye.

There was no obvious cause for his sudden death.

Microscopic Study: The brain, cord, and peripheral nerves, selected organs, and pieces of other organs were fixed in formol-saline. Stains for the nervous system were hematum and eosin and the Loyez iron hematoxylin, Busch, and Weigert-Pal methods.

No abnormality was found in any of the sections of the meninges, cerebral cortex, basal ganglia, or peripheral nerves. No perivascular cuffing was seen. Sections of nerve roots were not available for study.

The medulla showed neuronal degeneration of all degrees. Some of the cells appeared to be intact, while others were shrunken and distorted and had undergone varying degrees of destruction of nuclear detail. In many the nuclear material was fragmented, and its normal staining properties were lost. The white matter of the medulla showed spongiosis and a varying degree of demyelination, which was not of tract distribution.

Similar changes, but of less severity were seen in the pons and cord.

Sections of skeletal and cardiac muscle showed hyaline degeneration of isolated muscle fibers.

Case 2.—This woman, a housewife aged 38, had been in fair health since 1955, when she had undergone right pneumonectomy for tuberculosis. On Oct. 15, 1957, she attended her doctor's surgery, complaining of numbness of her hands and feet. A week earlier she had had a short feverish illness, which she called "the 'flu.'" Her doctor had found no muscle weakness; reflexes were brisk and plantar responses flexor. On Oct. 18 she became worse; her nose and face were numb, and all her limbs felt weak. That night she had difficulty in swallowing and complained that her tongue was numb. By the evening of Oct. 20 her breathing was becoming distressed, but her relatives did not summon her doctor until next morning, when she was found to be in extremis, dying before the ambulance arrived to take her to hospital.

Her body was brought to Cardiff Royal Infirmary, where, four hours after death, blood for virus serology was obtained from the right external jugular vein, using aseptic technique.

Pathology.—Autopsy, 24 hours after death, revealed right pneumonectomy and thoracoplasty and left basal bronchopneumonia. The gross appearance of the nervous system was normal.

Microscopic examination demonstrated changes in the nervous system similar to those seen in Case 1. The peripheral nerves, meninges, cortex, and basal ganglia were normal. In the midbrain, medulla, and at all levels of the spinal cord there was evidence of neuronal degeneration. In this case the lesion was severest in the spinal cord.

Virus Investigations

Case 1.—Serum taken two days before death gave a complement-fixing (C.F.) titer of 1/32 to influenza A virus and less than 1/8 with influenza B, influenza C, Q-fever, mumps, psittacosis, adenovirus, and Sendai antigens. Cold agglutinins and Streptococcus MG agglutinins were absent. The Paul-Bunnell reaction was negative.

Hemagglutination inhibition (H. I.) was carried out by the technique recommended in W. H. O. Technical Report Series No. 64.[44] The titers obtained against the Asian, Scandinavian, Eire, and Dutch strains of influenza A virus were respectively 1/32, 1/8, less than 1/4, and less than 1/4.

Influenza A (Asian strain) virus was isolated from both lung tissue and cerebrospinal fluid taken six hours after death.

Case 2.—A specimen of serum taken post mortem gave a C. F. titer of 1/64 to influenza A virus. The remaining examinations, like those for Case 1, were negative. H. I. gave titers against the Asian, Scandinavian, Eire, and Dutch strains of influenza A virus, respectively, of 1/32, less than 1/4, 1/4, and less than 1/4.

Specimens of cerebrospinal fluid were taken aseptically from the cisterna magna and the lumbar sac four hours after death. The former specimen was blood-stained, and from it influenza A virus (Asian strain) was isolated. No virus was isolated from the clear fluid of the lumbar sac.

The influenza viruses were isolated by the inoculation of 10% suspensions of pathological material into the amniotic cavities of 10-day-old embryonated eggs. After three days' incubation at 35 C, the amniotic fluids were harvested, and a further amniotic passage was made.

All strains showed hemagglutinating activity after this passage. Characterization was performed by means of immune ferret sera in hemagglutination-inhibition and hemadsorption-inhibition tests.

Comment

Among the reports of the recent pandemic which have been published in Great Britain, a few have described neurological complications. In most of these the illness was an encephalitis (Dubowitz,[9] 1958; Dunbar et al.,[10] 1958; Flewett and Hoult,[12] 1958; Guthrie et al.,[17] 1957; Holland,[19] 1957; McConkey and Daws,[28] 1958; McGill and Goodbody,[29] 1958; Meldrum et al.,[30] 1957; Morgan and Pickup,[33] 1958; Stephens and Cappell,[41] 1958; Watson,[43] 1957). Edmundson and Hodgkin[11] (1957) reported a single case of multiple peripheral neuritis which they saw in Yorkshire, and Compton Smith[7] (1958) described the case of a 13-year-old boy with symptoms and signs of polyneuropathy and involvement of the brain stem. From Singapore, Swee and Dourado[39]

(1957) referred to a 3-year-old girl who had tremor and ataxia of her limbs two months after the onset of her illness. The cerebrospinal fluid was normal. These authors stated also that they had seen other children with considerable weakness of the legs lasting one to two months. It is particularly interesting to contrast their report with that of Lim and his colleagues [26] (1957) from the same city. They had a series of 298 cases of Asian virus infection, of whom 39 had complications; but they make no mention of involvement of the nervous system. Flewett and Hoult [12] had two cases of ascending paralysis. They thought that the etiological relationship between neurological disorder and infection with Asian virus was unproved. Their Case 4 could scarcely be considered an example of Guillain-Barré syndrome.

Mogabgab [32] (1958), reviewing the features of the epidemic in the United States, referred to delirium and postinfectious encephalitis but stated that the virus had not been recovered from the central nervous system of man. Schreiber [38] (1957) had no neurological complications among his patients. Horner [22] (1958), however, reported five cases with involvement of the nervous system, in one of which, that of an 8-year-old boy, ataxia developed on the 13th day of illness. Recovery was complete within a fortnight. The initial pleocytosis and absence of increased protein content of the cerebrospinal fluid were points against the diagnosis of Guillain-Barré syndrome. Bell and his colleagues [2] (1958) reported a single case of encephalitis and referred to 12 others occurring during the epidemic.

In few of the earlier reports, despite the frequent references to an initial influenza-like illness, has any definite correlation with a specific virus been made. The single case of Jennings [23] (1952) has already been cited. In an excellent clinical account of "infections of the nervous system occurring during an epidemic of influenza B," Leigh [25] (1946) described a pattern of syndromes very similar to those which have been seen in South Wales. Unfortunately, he was unable to confirm recent viral infection in any of his nine cases, five of which had a polyneuritic syndrome. The cases of Hollander [20] and of Laha and Mitter [24] (1945), which were cited by Jennings [23] as examples of influenzal polyneuropathy, have no real relationship to this infection. None of these cases had viral studies; the adjectives "influenzal" and "grippal" were used to describe febrile prodromata.

The morbid histology of the Guillain-Barré syndrome has been extensively studied. The present trend of opinion has been amply summarized by Haymaker and Kernohan,[18] who have reviewed the older literature and added their own observations on the pathological material from 50 cases. They state:

> The disorder is characterised by a polyradiculoneuropathy which may begin in any peripheral neurons, spinal or cranial, circumscribed or widespread, may affect predominantly the motor or the sensory neurons or both to the same degree; it may remain essentially a radicular disorder, or, according to some authors, it may extend into the central nervous system at any point, and either ascend or descend, the outcome usually being dependent on the degree of involvement of respiratory or cardiac nerves.

In their view, the changes in the neuraxis were largely secondary to the extensive lesions of the peripheral nervous system. In earlier reviews, Roseman and Aring [37] (1941) and Pullen and Sodeman [35] (1946) had drawn attention to the central changes, but, like Haymaker and Kernohan,[18] had considered them secondary.

The central changes, which were also a feature of the two cases of this report, were fully described by Roseman and Aring.[37] In the spinal cord, they found that the cervical and thoracic regions were most severely affected, the ventral gray columns bearing the brunt of the injury. They described degenerative changes in the anterior horn cells, patchy outfall of cells from Clarke's column, mild glial reaction involving chiefly the oligodendroglia, and a small but significant increase in the ependymal cells surrounding the central

canal. In the brain stem the changes were similar, with a somewhat selective involvement of nuclear masses. The most advanced changes were seen in the olivary nuclei, whereas the hypoglossal nuclei escaped most lightly. Intermediate degrees of damage were seen in the cells of the tractus solitarius, the nucleus ambiguus, and the dorsal motor nuclei of the vagus. Most rostrally, the facial nuclei were the site of the severest changes. The funiculi of the vagus and hypoglossus showed both in their intramedullary and in their extramedullary course changes similar to those found in the spinal roots; it is interesting to correlate this with the authors' observation that of the brain-stem nuclei involved, the hypoglossal nucleus "contained the least pathology." Furthermore, the frequent finding of involvement of the dorsal motor nuclei of the vagus and the advanced changes in the vagal funiculi are especially interesting, in view of the high fatality rate of this disorder in some series. One of the patients in this report (Case 1) had learned to whisper after his tracheostomy and was conversing with his nurse when his pupils were seen to dilate, his pulse became imperceptible, and he died. Major obstruction of a bronchus, a frequent cause of sudden death in patients having assisted respiration, was not found at autopsy, and central involvement of the vagus or its axons might be postulated as the immediate cause of death. The histological studies showed that the severest lesions were present in the medulla of this patient.

The isolation of a virus from a body fluid or from a tissue, taken with the most stringent aseptic precautions in life or post mortem, is no guarantee against accidental contamination. This risk, always present, must increase enormously during a period when infection with that virus is epidemic. At the time at which the present cases were under investigation, clinical influenza was widespread among the hospital staff and postmortem examinations were being made daily in cases of proved influenza.

The demonstration of recent infection with Asian virus in these two fatal cases of the Guillain-Barré syndrome is, perhaps, unique, but we wish to emphasize our own view that the correlation should not be too readily accepted as indicating etiological relationship. The syndrome is not rare, and cases are commonly seen in the autumn and winter, according to Roseman and Aring,[37] though others have not found a special seasonal incidence. Two fatal cases occurring in rapid sequence would ordinarily cause little comment. In neither case could we demonstrate that Asian virus was causative; but the occurrence of these two cases at the height of the epidemic in Wales, which reached its peak during the week beginning Oct. 5, 1957 (Martin,[27] 1958), was so striking, together with the serological confirmation of recent infection with Asian virus, that we considered the correlation probably significant.

Summary

Two fatal cases are reported of the Guillain-Barré syndrome, occurring in relation to recent infection with the Asian strain of influenza A virus.

Dr. J. D. Spillane permitted us to publish details of Case 1.

Cardiff Royal Infirmary.

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Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Irving J. Sands, M.D., President, New York Neurological Society, Presiding

Combined Meeting, April 14, 1958

Therapy of Myasthenia Gravis. Dr. Paul F. A. Hoefer.

The present state of therapy of myasthenia gravis was reviewed.

The main abnormality of the disease is a deficit in the acetylcholine mechanism at the neuromyic junction, due to an excess of cholinesterase, an enzyme which hydrolyzes acetylcholine. The clinical disturbance is weakness and abnormal fatigability, due to an impairment of impulse transmission from the nerve to the muscle.

The conventional treatment with short-acting anticholinesterase drugs was evaluated; the advantages and disadvantages of these drugs, neostigmine, pyridostigmine, and ambenonium chloride, were analyzed. Two groups of long-acting compounds were also discussed. Alkyl phosphates are highly toxic, but at least one substance in this group (OMPA) was found highly useful in stable cases. Polymethylene-chain-linked double molecules of neostigmine and pyridostigmine are much less toxic and are promising for even maintenance of strength in myasthenia.

The different side-effects of all cholinergic drugs were described. They are muscarinic, nicotinic, and curariform in action. Muscarinic side-effects are managed by the use of drugs of the atropine series.

The management of respiratory crisis in myasthenia requires special measures. The rationale and results of thymectomy are uncertain at this time.

Discussion

Dr. David Nachmansohn: Dr. Hoefer has well outlined the importance of the acetylcholine system in myasthenia gravis and the interest of anticholinesterase drugs in therapy. The system is complex because at least four proteins are involved. Some progress has been achieved by analysis of molecular forces in the active surface of the proteins. This was the basis of the development by I. B. Wilson of the compound pyridine aldoxime methiodide. This drug completely and rapidly reverses the action of alkyl phosphates, which are powerful and virtually irreversible inhibitors of cholinesterase, and thus permits the use of this type of compounds in the treatment of myasthenia gravis.

The Electroencephalogram in Severe Brain Injury. Dr. Harry A. Kaplan and Dr. Albert W. Cook.

Observations were made on the state of consciousness and the EEG in patients who have sustained closed craniocerebral injuries but who have no overlying compressive mass, such as a subdural or an epidural hematoma. All had had an electroencephalogram within 24 hours following injury. Available evidence indicates that stupor may be related to injury of one or of several regions of the brain and that a dissociation between behavioral and EEG patterns may be obtained.

The present study suggested that the patients with this dissociation probably had the site of major neurophysiological dysfunction in the region of the diencephalon.

General Considerations on the Diagnosis of Brain Tumors by Cerebral Angiography. Dr. Juan M. Taveras.

Cerebral angiography has largely replaced pneumography in the diagnosis of supratentorial mass lesions. The advantages of angiography are as follows: (*a*) It does not disturb the intracranial pressure. (*b*) It permits the diagnosis of vascular as well as neoplastic lesions. Saccular aneurysms, and sometimes arteriovenous malformations, may look like a mass lesion on air studies. (*c*) Angiography permits a more accurate localization of hemisphere lesions than pneumography; that is, the surgical exploration may be directed to a smaller area of the brain. (*d*) It is often possible to decide preoperatively whether one is dealing with an intra- or an extracerebral lesion. (*e*) When abnormal vascularity is present, localization is extremely accurate, and the histologic type, that is, whether one is dealing with a malignant intracerebral lesion or with a meningioma, can be predicted accurately in over 90% of cases. Serial films made routinely are necessary to increase the accuracy of diagnosis.

In the cerebral hemisphere the most suitable locations for diagnosis are the frontal, temporal, and parietal region. Angiography has been disappointing in the diagnosis of posterior-fossa tumors, and it cannot demonstrate intraventricular tumors. Angiography gives scanty information in tumors of the corpus callosum and thalamus. When no localizing signs are present, pneumography is to be preferred, except perhaps when multiple metastases are suspected, because, at times, they show abnormal vascularity. It should be kept in mind that one diagnostic procedure should not be carried out to the exclusion of the other; both procedures often have to be performed in many patients.

Discussion

DR. SIDNEY W. GROSS: The deep cerebral veins are often of great importance in localizing lesions, which sometimes are not localizable from the arterial circulation alone.

Angiography is very efficient in the diagnosis of subdural hematomas, where the diagnosis can be made with almost 100% accuracy. Angiography often discloses avascular zones, indicating a cyst or a large intracerebral clot with the absence of vessels. Whether to do angiography or pneumography depends first on the individual case. Occasionally it is of great value to have air in the ventrimular system and then do angiography, so that the relationship of the vessels to the ventricular system is demonstrated.

DR. JUAN M. TAVERAS: We, of course, are very much aware of the value of the deep veins in the diagnosis of masses by angiography. If I were going to choose between air study and angiography in diagnosis of a thalamic tumor, I should choose air study, because, while I have diagnosed a considerable number of thalamic tumors when angiography was carried out, some thalamic tumors, even large ones, do not cause any deformity because they do not grow in a direction in which they will displace the internal cerebral vein or the basilar vein. For the latter reason, therefore, I should say that for these deeply placed tumors angiography is less satisfactory than pneumoencephalography.

I did not mention subdural hematoma because the advantages of angiography are so well known that it did not have to be mentioned separately, but it is worth while pointing out.

Vascular Malformations of the Spinal Cord. DR. SIDNEY W. GROSS and DR. BRUCE L. RALSTON.

The clinical, radiological, and pathological observations in 10 patients with vascular malformations of the spinal cord revealed the following. The disorder is found mainly in middle-aged or elderly men, although 2 of the 10 patients were women and one patient was 15 years of age. Low-back pain of a nondescript character is often present for many years prior to the development of weakness in the lower extremities, which is the symptom most often causing the patient to consult a neurologist. The weakness in the lower extremities develops gradually in most patients. In 3 of 10 patients, however, paraplegia developed within a matter of a few hours. Every patient in this group had myelography, and this was followed by surgical intervention. In several the diagnosis of a vascular malformation was suspected from the abnormalities in the myelogram, which showed bizarre defects, manifested by tortuous, circular, corkscrew-like, irregular, branching, and serpiginous defects. Lumbar puncture in most of the cases disclosed a clear spinal fluid with normal dynamics. However, in two patients a complete block was present, and in one, an incomplete block. The protein in the spinal fluid varied from 41 to 330 mg. %. The results of surgical treatment in this series were disappointing. Nevertheless, one patient, who was followed for more than 10 years, improved markedly after surgical intervention and, when last seen, was still in fairly good condition. Laminectomy is probably indicated only in those patients who have a complete block on manometric study or myelography.

Discussion

DR. LESTER A. MOUNT: We are all indebted to Dr. Gross and Dr. Ralston for bringing to our attention again so clearly the pathology, symptoms, signs, and diagnosis of these interesting vascular lesions. I think one word of warning to the neurosurgeon may be in order; that is, sometimes there are dilated veins and arteries above or below a spinal cord tumor, and one can get a false impression at the operating table of the presence of vascular malformations, when they are nothing more than dilated arteries or veins associated with a spinal cord tumor that may be a little above or below it.

DR. ALBERT WILLIAM COOK: In the group we have encountered, we have had only one instance in which bruit occurred. I wonder whether Dr. Gross will comment on the presence of bruit over the site of the lesions he presented.

DR. I. M. TARLOV: The prognosis being unfavorable in these cases, one wonders whether it might be improved by removing some of these lesions. We have had experience with one spinal vascular lesion which looked so forbidding at operation that we promptly backed away from it. The patient then became almost completely paralyzed, so we reoperated. At operation angiography was done, iodopyracet (Diodrast) being injected into the lesion, using a portable x-ray machine.

We were thus able to identify the entering arteries and the emerging veins and remove the lesion, which turned out to be a hemangioblastoma. Complete motor and almost complete sensory recovery followed. Might not, therefore, angiography at operation also facilitate removal of some vascular malformations of the spinal cord?

DR. BRUCE L. RALSTON: In reply to Dr. Cook's question, no bruit was heard in this series, although I am not sure how many times it was listened for.

Dr. Tarlov has commented on the use he made of angiography during operation on a vascular lesion of the spinal cord. If these lesions are like their cerebral counterparts, then they may have a hypertrophied arterial input, the shunt itself, and dilated, arterialized veins. The surgeon, facing a tangled mass of vessels at surgery, is unable to determine the various components of the malformation. He lacks a preoperative angiogram and the advantage of a well-defined and spatially extended system of arteries and veins, such as is seen in the cerebrum. We have little hope of improving our diagnosis and treatment of vascular malformations of the spinal cord unless they can be studied dynamically by angiography. A recent article (Höök, O., and Lidvall, H.: Arteriovenous Aneurysms of the Spinal Cord: A Report of 2 Cases Investigated by Vertebral Angiography, *J. Neurosurg.* 15:84-91, 1958) has shown it is possible to visualize upper cervical lesions by vertebral angiography. We have attempted to fill a portion of lower lesions by injection of diatrizoate (Hypaque) into the overlying spinous process, without success. It would seem that some form of aortography, safely applied, will be necessary for this purpose.

Pharmacogenic Vs. Electroshock Therapy for Melancholia. DR. THEODORE R. ROBIE.

In 1957, for the first time, a chemotherapeutic agent, iproniazid (Marsilid), was proved efficacious in overcoming melancholia in most cases. It has striking advantages over electroshock, since most patients continue at work while the chemical induces return of former efficiency, skill, and well-being. There is no EST-induced amnesia, and no skeletal-fracture complications.

An average patient is administered 150 mg. daily of the drug for the first week, and thereafter the dose is reduced gradually, 50 mg. or less being given daily by the fourth week. Most patients do not show remission until they have been taking the drug for a period of four weeks; but when they respond, their enthusiasm for what has been accomplished by chemotherapy is unrestrained. The use of any chemical involves certain hazards, and iproniazid is no exception. The known possible side-effects must be watched for and quickly controlled by protective measures. Edema, occurring in 3% to 5% of cases, can be quickly overcome by chlorothiazide (Diuril), and iproniazid resumed in smaller dose. Temporarily reduced libido (rare) usually responds to reduction in dosage, or to pantothenic acid in large doses, or both. Hypotensive effect is an almost universal phenomenon, necessitating reduction in dosage, or sometimes temporary cessation of drug therapy until blood pressure has returned to normal. In rare cases it may be necessary to give cortisone temporarily when hypotension is persistent. Although hepatitis is reported, and deaths due to this allegedly have occurred, authoritative pathologists insist that the hepatitis observed cannot be differentiated from virus hepatitis. I believe that hepatitis can be averted by care in preventing excessive hypotension. Agranulocytosis, encountered occasionally with any modern chemical therapy, has been reported rarely. Since mortality is 1 per 1,000 treated cases when electroshock is administered, and only 1 per 16,000 under iproniazid therapy, obviously chemotherapy is safer. Therefore iproniazid chemotherapy can be expected to come into wide usage.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND NEW YORK NEUROLOGICAL SOCIETY

Morris Herman, M.D., Chairman, Section of Neurology and Psychiatry, Presiding

Combined Meeting, May 22, 1958

Use of Retinal Arterial Pressure as a Diagnostic Tool in Internal Carotid Artery Disease. DR. ELLIOT D. WEITZMAN and DR. HAROLD SPALTER.

This study is concerned with the evaluation of the Baillairt ophthalmodynamometer as a diagnostic tool in spontaneous occlusion of the internal carotid artery. Of 11 cases of occlusion, 9 demonstrated a significant lowering of the retinal artery pressure on the side of the occlusion. In one case in which the occlusion was above the orifice of the ophthalmic artery, the pressure was higher on the side of the thrombosis. One case with occlusion proved by arteriography three years before had equal pressures on the two sides. On the occluded side the pressure was lower by an average of 43% systolic and 50% diastolic. The least reduction was 22%

and the greatest 84%. Four patients of this group underwent endarterectomy, with removal of both clot and intimal plaques. Three had no significant change in postoperative pressure readings. The fourth had a dramatic rise in pressure postoperatively to become equal to that of the unaffected side.

In addition, measurements were made in a control group of 19 patients with other neurologic conditions in whom internal carotid artery occlusion was initially considered in the differential diagnosis. In this group the average pressure difference between the retinal arteries was 3% systolic and 4% diastolic. The greatest difference was 13%. On the basis of the above findings, we have chosen a difference of 20% in either diastolic or systolic pressure as being the upper limit of normal.

The Baillairt ophthalmodynamometer is a useful tool for the diagnosis and evaluation of the medical and surgical management of spontaneous internal carotid artery occlusive disease.

A Pilot Study of Aspects of the Earliest Memory. DR. ROBERT J. LANGS.

This paper is concerned with an ongoing study of the first childhood memories of 300 psychiatric patients and 150 other patients drawn from the medical, surgical, and obstetrical services. Our goals have been, first, to collect a series of earliest memories large enough for a multifactorial analysis; second, to develop descriptive and quantitative parameters for these memories; third, to differentiate and classify earliest memories; fourth, to study the question as to whether such memories change with time, and, fifth, to explore the relationship between earliest memories and a wide variety of other clinical phenomena, including dreams, psychodynamics, interpersonal relationships, self-image, level of psychosexual development, and defensive operations.

Our preliminary impressions of the material collected to date are presented in the light of the literature on early memories. Important data can be extracted from these memories. To cite a few brief examples, this includes the current needs of the patient (e. g., impregnation themes are common in first memories from pregnant women), diagnostic clues (e g., first memories in the form of dreams have been reported only by schizophrenic patients), and aspects of the patient's perception of significant others and the world as a whole.

The relationship of earliest memories to data gained from psychological tests and from the patient's dreams is a complex one which we are exploring. We have also been interested in memories which are reported in color (about 10% of the memories in our sample, usually reported by women), and in nonvisual first memories (most frequent in very disturbed patients). It appears, too, that over a period of 6 to 10 months the main content of the earliest memory remains essentially unchanged, though subtle differences appear which may be of great significance. In acutely psychotic patients the first memory may be different from one week to the next. Our data indicate that earliest memories are of considerable clinical, theoretical, and heuristic value.

Neuropsychiatric Mainfestations of Hypercalcemia. DR. GERARD M. LEHRER.

Not infrequently a patient may present with confusion, lethargy, and a bizarre organic mental syndrome as the primary expression of hypercalcemia, regardless of etiology. Three cases are reported which were referred for neurologic consultation because of a peculiar organic mental syndrome—a clinical picture which caused much diagnostic confusion until a high serum calcium level was established as the etiologic factor. In two of the patients fluctuations in the serum calcium levels were observed to be correlated with changes in mental status, confusion increasing with rise in the serum calcium level. The underlying causes of the hypercalcemia in the three patients were, respectively, hypervitaminosis D, Hodgkin's disease, and parathyroid adenoma. It is emphasized that neuropsychiatric symptomatology may be the presenting picture in a hypercalcemic syndrome. Since prolonged hypercalcemia may cause severe renal tubular damage, and even death, and since in most cases therapeutic measures are available for either eliminating the primary cause of the hypercalcemia or lowering the serum calcium level, e. g., by edathamil, early diagnosis is extremely important. The possibility of hypercalcemia should, therefore, be borne in mind in the differential diagnosis of organic mental syndromes of obscure etiology.

Evaluation of the Sedation Threshold Test. DR. DONALD BOUDREAU.

A neurophysiological test, the sedation threshold, has recently been described as an objective method of determining clinical psychiatric data. Specifically the sedation threshold has been correlated with two psychiatric variables, manifest anxiety and degree of ego impairment. From a practical point of view, this test has been considered to be a method of determining the degree of manifest anxiety in psychoneurotics and a means of differentiating various diagnostic categories, particularly between neurotic and psychotic depressions. The present study was undertaken to examine the validity of these findings and to evaluate the stability of the threshold as an enduring biological characteristic of the individual. The test procedure was similar to that described by Shagass, except for several minor modifications. The subjects were chosen for the degree of manifest anxiety demon-

strated and the diagnostic category into which they fell. A total of 60 tests were performed on 36 patients and 3 controls. In this series of tests there was found to be no correlation between the sedation threshold and the degree of manifest anxiety as clinically determined by two psychiatrists. In addition, the sedation threshold had little stability when performed on two nonpatient controls and one psychiatrically ill patient whose psychopathology did not vary over the period of testing. There was, however, some correlation between the threshold and various diagnostic categories, particularly psychotic and neurotic depressions. It was concluded that, because of various technical difficulties, the sedation threshold was difficult to determine, and often equivocal. While no correlation was found between the threshold and manifest anxiety, it was felt there was some evidence of its validity in the determination of the degree of ego impairment as described by Shagass.

Anorexia Nervosa in a Twelve-Year-Old Girl. Dr. Lawrence Loeb.

Anorexia nervosa has been descriptively placed in various diagnostic groups. In the bulk of source cases for discussion of the syndrome treatment was instituted after the process had existed for some time. The case described is that of a 12-year-old girl hospitalized at the New York Hospital, Westchester Division, without prior treatment.

The patient had been hospitalized after a 40-lb. weight loss in a three-month period. Her background is described briefly, as are some of the factors the author thinks dynamically important in the development of this illness in the patient. Physical work-up, including neurologic examination, skull films, and electroencephalogram, were all found to be within normal limits.

Anorexia nervosa is seen to be, in a simplified fashion, an acting out of the wish not to grow up, to remain always the favored child, unthreatened by the demands of sexuality, of adulthood and its attendant responsibilities.

Remarkable in this case is the relative preservation of a neurotically compromised, but otherwise intact, personality.

Three Cases of Gilles de la Tourette's Syndrome Treated with Psychotherapy and Chlorpromazine. Dr. Alvin M. Mesnikoff.

Gilles de la Tourette described this uncommon syndrome, having the following triad of symptoms: multiple tics, involuntary explosive coprolalic utterances, and echo phenomena. The present report, based on three schizophrenic male patients followed for three years, focuses on (1) the parent-child relationship with specific attention to neuromuscular development and (2) treatment with psychotherapy and chlorpromazine.

The family histories emphasized maternal dominance. The mother's conflict concerning male-female sex roles was reflected in the handling of their male infants. Female siblings, one in each family, were reasonably well adjusted. The mothers demanded superior performance, but were punitive and restrictive toward assertive and exploratory behavior expressed in motor activities. This activity was misinterpreted as aggressive and defiant and became the focus for the mother-son struggle. This emphasis appeared to be a factor in the later selection of the neuromuscular system for the symptomatic expression of intrapsychic conflict.

Psychotherapy alone resulted in improvement, but increased stress caused exacerbation of the tics, thus undermining the patient's self-confidence. Chlorpromazine helped to relieve tension, permitted greater control of the tics, and reduced the patient's fear of being helpless in dealing with them. The drug appeared to serve as an ego accessory and supported more meaningful utilization of the insight and support derived from the psychotherapy.

A 25-year-old patient with a 15-year history had considerable relief of his tics; but when confronted with reality demands concerning a job, he became fearful and paranoid and withdrew from treatment. Two adolescents have minimal tics. They live at home, attend school, and are continuing in psychotherapy, using the drug as necessary.

PHILADELPHIA NEUROLOGICAL SOCIETY

Harvey Bartle Jr., M.D., Presiding

Regular Meeting, Dec. 6, 1957

Pyridoxine Metabolism and Convulsive Seizures. Dr. George D. Gammon and Mr. Robert Kamrin (by invitation).

Methoxymethylpyridoxine will produce seizures in a variety of animals and in man. These may be prevented or stopped by the administration of pyridoxine (vitamin B_6) in two to three times the dose required for seizures. Thus, by this drug, an acute pyridoxine deficiency can be induced. We have studied the effect of various intermediary

metabolites on the seizures induced by this drug. It was found that γ-aminobutyric acid, recently identified as Factor I, ameliorated or prevented these seizures. A variety of some 20 other intermediary metabolites, particularly in the amino acid series, failed to give this protection, as did other ω-amino acids, which have been found to have a sedative action, resembling gaba. The evidence is consistent. The interpretation is that an inhibitory action on glutamic decarboxylase may be involved in the production of the seizure.

Discussion

DR. NATHAN S. SCHLEZINGER: I was wondering whether there was any practical application. Were different types of animals or patients with various type of seizures utilized in this study?

MR. ROBERT KAMRIN: We have observed that the administration of methoxymethylpyridoxine to animals that have no known neurological lesions results in convulsions that begin with a twitching of the facial muscles and extends to generalized tonic-clonic convulsions. Patients who have a previous history of focal seizures, however, react to methoxymethylpyridoxine with focal seizures. It thus seems that we possibly have an agent that can reproduce a patient's usual seizure pattern.

DR. GEORGE D. GAMMON: One patient had a temporal-lobe focus. We have not tried many types of cases. We are asking whether there is a variety of seizures with differential sensitivity to this material. Will γ-aminobutyric acid stop human fits? It does so in these animals. This pyridoxine antagonist may have a practical application in electroshock therapy. One schizophrenic woman developed hallucinations. We do not know the meaning of this.

Surgical Treatment of Involuntary Facial Movements. DR. WILLIAM H. WHITELEY.

The purpose of this paper is to report the successful treatment of two different types of involuntary facial movements by means of deliberate peripheral section of the facial nerve, accompanied by immediate spinofacial anastomosis. One patient represented a problem in involuntary facial tic; the other had hemifacial spasm. The woman with the facial tic had suffered for 14 years and had been unrelieved by psychiatric care. Spinofacial anastomosis was performed during September, 1954, and when the patient was last seen, three and one-half years after operation, she remained free of her old facial tic. She was much pleased and had not developed any substitutive symptoms. The other patient had suffered with attacks of typical hemifacial spasm for 29 years. His disability was accentuated by blindness of the opposite eye, so that during the attacks of spasm (lasting about 30 to 60 seconds) he was virtually blind because of involvement of the orbicularis oculi muscle. Spinofacial anastomosis was performed in November, 1956; and when the patient was last seen, one year after operation, he was still free of all his hemifacial spasm and was greatly satisfied with the relief obtained. Traditionally, facial tic has been differentiated from hemifacial spasm in that the former is considered psychogenic and the latter organic in nature. A review of the literature, however, indicates that the exact cause of hemifacial spasm is still unknown. In view of the results obtained in these two cases, it would appear profitable to pursue this treatment in the future.

Discussion

DR. RICHARD G. BERRY: Was there any impairment of consciousness during the attacks in the last case?

DR. RUDOLPH JAEGER: Dr. Whiteley's results were excellent. Here is an interesting side-light on generalized unilateral facial tic of 13 years' duration. The patient was seen on Aug. 25, 1955. On Feb. 8, 1956, a spinal facial anastomosis was performed. On March 21, 1956, the patient said she was pleased with the result. On March 25, 1956, her face moved when she moved her shoulder. This is the customary interval for restoration of function. On Sept. 12, 1957, her face began to twitch again. When she moved her shoulder, her face also moved. Therefore, 19 months after the operation the patient again had mild facial ties, and partial voluntary movements of the face on facial expression and on shoulder movements. As far as I know, this is the first time it has been observed that a severed facial nerve may make contact with and regenerate into the facial nerve, along with regeneration of the spinal accessory into it. This is a satisfactory operation, and a mentally stable person will be satisfied with the result. If the patient is dissatisfied and the tic is preferred, it is possible to reunite the ends of the facial nerve. The tic is sure to return. To prevent regeneration of the facial nerve, it should be cut flush with the skull and a plug of bone forced into the stylomastoid foramen.

DR. WILLIAM H. WHITELEY: In answer to Dr. Berry's question, there was no lapse of consciousness during the patient's spasms in the last case. I want to thank Dr. Jaeger for his comments.

Inclusion-Body Encephalitis. DR. RICHARD G. BERRY.

Clinical and pathological descriptions are presented of three cases of encephalitis, each of which had in common intranuclear eosinophilic inclusion bodies of Cowdry's Type A. One case was clinically and pathologically similar to the cases of subacute inclusion bodies described by Dawson,

and to the subacute sclerosing leukoencephalitis of van Bogaert. The second case, characteristic of Schilder's diffuse sclerosis, had, in addition to the inclusion bodies, the pathological picture of subacute sclerosing leukoencephalitis and many features of the nodular panencephalitis of Pette-Doring. The third case of acute necrotizing encephalitis had some of the features of subacute sclerosing leukoencephalitis and nodular panencephalitis.

These three cases illustrate recent concepts in the literature which suggest at the least a continuum in the sporadic encephalitides: subacute inclusion-body encephalitis (Dawson); subacute sclerosing leukoencephalitis (van Bogaert); nodular panencephalitis (Pette-Doring), and certain cases of Schilder's diffuse sclerosis. In each of the author's cases, there was a panencephalitis, with varying degrees of gliosis and numbers of inclusion bodies. It is proposed that an infectious agent (or agents), presumably virus, affected the gray and white matter. In the acute case a necrotizing lesion resulted, whereas in the subacute cases the necrosis was less in evidence. From concomitant edema, and from hypoxia related both to edema and to thickening of blood vessel walls, further lesions in the subcortical white matter and centrum semiovale resulted. Sclerosing demyelination was the result of these factors, in addition to a possible focal attack on myelin, and the secondary demyelination of neuronal involvement.

Discussion

DR. GEORGE D. GAMMON: Was there any metachromasia in these three cases? Are any special techniques used? We recently had a child with myoclonic twitchings in Children's Hospital. On brain inoculation, Dr. George Seiden found no cytotoxic agents. Are urinary sediments of any value in the diagnosis?

DR. ALEXANDER SILVERSTEIN: I should like to ask Dr. Berry a question. Can one differentiate clinically inclusion-body encephalitis, Devic's disease, disseminated encephalomyelitis, and acute multiple sclerosis? Also, from the histopathologic standpoint, since the inclusion bodies can be so readily overlooked, are there any other distinctive features which can distinguish inclusion-body encephalitis from the other above-mentioned demyelinating disorders? I also wonder whether Dr. Berry would venture an opinion as to the mechanism of the decerebrate rigidity in the case reported.

DR. RICHARD G. BERRY: There was no evidence of metachromatic material in any of these cases. The metachromatic leukodystrophies are a separate entity, often heredofamilial, and probably related to Schilder's second case of diffuse sclerosis. Inclusion bodies can undoubtedly be found in some biopsy specimens by chance and diligent search with oil immersion. The diffuse, but spotty, sites of these inclusion bodies militate against 100% success. In retrospect, we were able to find one such cell in a biopsy specimen from the first case, but missed it on first review of the material. The subacute form of inclusion-body encephalitis may appear clinically like a disseminated encephalomyelitis, but optic neuritis is not present, and the hyperkinesias and dyskinesias of inclusion-body encephalitis are not present in acute multiple sclerosis. Microscopically, the lesions of inclusion-body encephalitis are diffusely spread through the white matter; the gray matter is involved in a chronic polioencephalitic process. The acute necrotizing encephalitis with inclusion bodies, as in our last case, is usually limited to the temporal lobes and base of the brain, with little or no evidence of spinal cord necrosis.

Abstracts from Current Literature

EDITED BY BERNARD J. ALPERS, M.D.

Peripheral and Cranial Nerves

DIABETIC NEUROPATHY: PITFALLS IN DIAGNOSIS. M ELLENBERG, A. M. A. Arch. Int. Med. 100:906 (Dec.) 1957.

Ellenberg describes the case histories of seven patients with diabetes who presented findings suggestive of diabetic neuropathy. In each case the specific problem could be related to pathology other than the diabetes, and the diagnostic spectrum included such entities as senile osteoporosis with compression of the lumbar spine, two cases of herniation of the intervertebral disk, nontropical sprue, osteitis deformans (Paget's disease), the Guillain-Barré syndrome, and osteomyelitis of the spine. The authors stress the importance of bilateral symptoms and predominantly sensory involvement of the lower extremities, especially with pain, as being particularly characteristic of diabetic neuropathy. This picture, taken in conjunction with associated elevated total protein of the spinal fluid, vascular changes and clear-cut diabetes, is most suggestive but not conclusive. The diagnosis will not in all probability be reached by a purely clinical approach, and the importance of additional laboratory and x-ray studies is particularly emphasized in view of the results described in this paper.

PARSONS, Montrose, N. Y.

PERONEAL PARALYSIS—A HAZARD OF WEIGHT REDUCTION. B. E. SPROFKIN, A. M. A. Arch. Int. Med. 102:82 (July) 1958.

Sprofkin describes nine middle-aged patients who, following relatively rapid and extensive weight loss, developed foot drop, steppage gait, and, in all but one case, foot inversion and sensory loss over the lateral leg and dorsum of the foot. All these patients were demonstrated to have the habit of sitting with legs crossed, thus compressing the common peroneal nerve between the ipsilateral fibular head and the contralateral femoral condyle and patella. In the one patient without significant sensory change or foot inversion, only the deep peroneal nerve was involved. Other neuropathogenic factors, such as alcoholism, were present in only two cases, and no patient was diabetic. Of the seven unilateral cases, five were left-sided and two right-sided, and in each instance involvement was found in the habitually crossed leg. Other activities tending to produce peroneal palsy, such as prolonged crouching, squatting, kneeling, or other types of sustained leg flexion, especially in thin persons, were reviewed. The importance of avoiding confusion between this relatively innocuous neuropathy and cerebral or spinal cord disease, on the one hand, and hysteria, on the other, is stressed.

PARSONS, Montrose, N. Y.

GASTRECTOMY COMPLICATED BY THE GUILLAIN-BARRÉ SYNDROME. D. ORRINGER, A. M. A. Arch. Surg. 76:447 (March) 1958.

A 62-year-old man had a subtotal gastrectomy for chronic gastric ulcer. The operation was carried out under intravenous and spinal anesthesia. Nine days after operation he developed rapidly progressive polyneuronitis, which culminated in tetraplegia and respiratory paralysis. Aided by early use of tracheotomy and a respirator, the patient survived and, after several months, made a complete recovery. The author felt that the neurologic syndrome had no causal relationship to the gastric ulcer and the spinal anesthesia.

LIST, Grand Rapids, Mich.

ISONIAZID AS A CAUSE OF OPTIC NEURITIS AND ATROPHY. I. KASS, W. MANDEL, H. COHEN, and S. H. DRESSLER, J. A. M. A. 164:1740 (Aug. 17) 1957.

The most frequent toxic symptoms and signs following isoniazid therapy are secondary to involvement of the nervous system. It appears that malnourished patients, chronic alcoholics, and persons with preexisting cerebral damage are particularly prone to the neurotoxic effects of isoniazid. In addition to the usual toxic manifestations, Kass and his co-workers observed two cases of optic neuritis, and eventually atrophy, after the use of isoniazid. In one, where the onset of visual difficulties occurred within two months after a marked increase in dosage, a dis-

continuance of isoniazid therapy brought reversal of the process. In the second, that of a malnourished alcoholic, the onset of visual difficulties occurred within one month after initiation of therapy with isoniazid. The use of isoniazid was discontinued, but the patient became completely blind, his condition deteriorated rapidly, and he died one month later. The authors assume that the optic lesions are part of the neurotoxic effects of isoniazid and, though rare, do not represent an unusual form of drug idiosyncrasy. Since serious visual disturbances may follow the use of isoniazid, it is imperative that ophthalmological examinations be conducted whenever visual complaints are voiced. This is important in view of the fact that the optic lesions are likely to be reversible if isoniazid therapy is discontinued promptly. It is also suggested that all patients receiving isoniazid should be given pyridoxine in a dose of 25 to 100 mg. daily to reduce the incidence of neurotoxic effects from isoniazid.

ALPERS, Philadelphia.

CERVICAL RIB AND THROMBOSIS OF THE SUBCLAVIAN ARTERY. H. SHENKIN, J. A. M. A. 165: 335 (Sept. 28) 1957.

Shenkin presents three patients who suffered subclavian arterial thrombosis as a complication of a cervical root syndrome. All three patients had had only mild symptoms for several years preceding the thrombosis. The thrombosis occurred without premonitory increase in symptoms. The author suggests that surgical intervention should be advised as a prophylactic, as well as a therapeutic, measure whenever a cervical rib produces even mild symptoms, and arterial compression in some positions can be demonstrated. Interruption of the sympathetic innervation to the upper extremity after thrombosis had occurred was clearly beneficial in this series of patients.

ALPERS, Philadelphia.

TRIGEMINAL NEURALGIA. J. G. RUSHTON and H. L. A. MACDONALD, J. A. M. A. 165:437 (Oct. 5) 1957.

In an attempt to learn something of the natural history of trigeminal neuralgia and to discover whether spontaneous remissions of pain are of such character as to create a problem in judging the effectiveness of a particular treatment for this condition, Rushton and MacDonald studied 155 cases seen at the Mayo Clinic in 1953. No patient with known intracranial tumor or aneurysm was included in the series. Analysis of these 155 cases showed that 78 patients had experienced one or more spontaneous remissions lasting 6 months or longer and that 38 had had similar remissions of 12 months or more. This finding may have explained some reports of good therapeutic results from a variety of treatments, such as remissions lasting up to four years in 17 out of 39 patients after the extraction of apparently sound teeth. The authors suggest that a period of observation of at least six months, and preferably one year, should elapse before the effectiveness of any treatment is judged. By so doing, the error imposed by spontaneous remission may be lessened. The time between the onset of illness and the presentation of the patient for his first treatment plus the duration of the longest spontaneous remission will give some clue to the expected future course of the illness. Patients who have had trigeminal neuralgia for a long time and who have enjoyed long remissions may find that their disease follows a somewhat benign course.

ALPERS, Philadelphia.

NERVE REPAIR IN CIVIL PRACTICE. O. R. NICHOLSON and H. J. SEDDON, Brit. M. J. 2:1065 (Nov. 9) 1957.

Nicholson and Seddon made a study of the end-results of nerve suture after 305 repairs in 277 patients, most of whom had suffered injury in the region of the wrist. The authors used the same method in their study of these civilian injuries as was employed for the assessment of recovery in the Report of the Nerve Injuries Committee of the Medical Research Council. In 198 of the 305 cases of suture repair, the patients had been observed for three or more years postoperatively. Recovery occurred within less than three years in many patients. Useful motor recovery occurred in two out of three sutures of the median nerve in injuries at the level of the wrist, and sensory recovery was good in four out of five. Useful sensory and motor recovery followed ulnar-nerve suture in four out of five cases, and in one out of three some degree of independent lateral movement of the fingers was regained. Recovery was better in children than in adults. The extent of the gap to be sutured was much smaller than in military injuries; an autogenous graft to repair the nerve was required in only 21 instances. There was evidence that extensive mobilization adversely affected the prognosis.

Delay of six months, or even more, between injury and nerve suture was still compatible with recovery. The authors believe that the reason for this may be that most of the lesions were distal, so that the distance to be covered by the outgrowing axons was not great. The authors consider secondary suture more reliable than primary suture. They give the following technical reasons for this: Intraneural damage, when it occurs, is much easier to recognize some weeks after injury that at the time, because it appears as a palpable, and, on section, visible, zone of intraneural fibrosis. Also, the epineurium becomes thickened after injury, so that in a few weeks it is an ideal structure for holding fine sutures. The authors advise repair of associated damage to tendons at the time of injury, with simple approximation of the severed nerves.

ECHOLS, New Orleans.

Treatment, Neurosurgery

INTRATHECAL AMETHOPTERIN IN NEUROLOGICAL MANIFESTATIONS OF LEUKEMIA. J. A. WHITESIDE, F. S. PHILIPS, H. W. DARGEON, and J. H. BURCHENAL, A. M. A. Arch. Int. Med. 101:279 (Feb.) 1958.

The authors experimentally demonstrate tolerance of up to 0.5 mg/kg. of intrathecal amethopterin in dogs. They were successful in temporarily controlling the neurological manifestations of five children with leukemia and lymphosarcoma in doses ranging from 0.1 to 0.5 mg/kg. of intrathecal amethopterin. The drug was well tolerated but produced megaloblastosis and a mild depression of the marrow count. No signs of meningeal irritation occurred, and the improvement in neurological status, which lasted from one to six weeks, was reflected in the clinical examinations, as well as in electroencephalograms. In all instances cerebrospinal fluid levels were much in excess of those obtained with other methods of administration, and two children previously considered refractory to the drug exhibited favorable response.

PARSONS, Montrose, N. Y.

EFFECT OF THERAPEUTIC MOBILIZATION ON HYPERCALCIURIA FOLLOWING ACUTE POLIOMYELITIS. F. PLUM and M. F. DUNNING, A. M. A. Arch. Int. Med. 101:528 (March) 1958.

The effect of various therapeutic mobilization procedures on hypercalciuria associated with extensive paralysis in a group of 37 poliomyelitis patients was evaluated. The procedures employed included the rocking bed, tank exercises, sitting, standing and walking with and without crutches. In none of the subjects was there significant decline in hypercalciuria which could be attributed to mobilization, nor was there any apparent influence exerted on the progressive osseous dimineralization seen in the more severely involved patients. In view of the stress on early mobilization in the prevention of osteoporosis, renal caculi, and pseudohyperparathyroidism in paralyzed patients, these observations are of interest. The apparent paradox suggested by previous observations on hypercalciuria in normal persons subjected to immobilization procedures (i. e., being placed in casts) with amelioration following mobilization would seem to be explained in terms of the relatively constant tension exerted by normal skeletal muscle activity during waking hours despite immobilization.

PARSONS, Montrose, N. Y.

PSYCHOMETABOLIC CHANGES IN PHENYLKETONURIA TREATED WITH LOW-PHENYLALANINE DIET. H. MEYER, E. T. MERTZ, H. E. STADLER, H. LELAND, and J. CALANDRO, A. M. A. Arch. Int. Med. 101:1094 (June) 1958

A low-phenylalanine diet was administered to three out of a group of six children with phenylpyruvic oligophrenia. Periodic evaluations were performed over a six months' period, using electroencephalographic and clinical observations and specialized quantitative biochemical and psychological techniques. The biochemical studies included the phenylpyruvic acid-creatinine ratio and monthly serum phenylalanine; psychological studies consisted of the Wallin Peg Boards, the Columbia Test of Mental Maturity, and the Vineland Social Maturity Scale. At the conclusion of the six months' period the diets of test and control children were reversed, and the evaluations were repeated over a two and one-half months' period. There was evidence that the low-phenylalanine diet resulted in biochemical changes; there was a fall in the urinary phenylpyruvic acid-creatinine ratio and in serum phenylalanine levels. Psychologically, there was uneven improvement in functional efficiency with increased socialization and decreased autism. In one test case there was a notable decrease in frequency and severity of epileptic seizures. All favorable changes seen in test children were noted to recede upon restitution of

regular diet, and the controls given the low-phenylalanine diet displayed the evidences of improvement just described. The smallness of the sample and the reputed wide discrepancy of ages represented constituted obstacles to the interpretation of results. The age factor was especially relevant in terms of the biochemical observations demonstrating the variation of the phenylpyruvic acid-creatinine ratio with age (less with younger children). In view of this fact, it would have been desirable to mention the ages of the matched children, the discrepancies in age, and other modifying factors (presence or absence of other congenital abnormalities affecting development, convulsive siezures, spasticity, microcephaly, etc.) which the authors indicate must be "reckoned with." The paper lacks a summary. Conclusions straggle through the report, thus necessitating repeated review of each individual section (including that on "Diet," which gives the ages of the three test children, as well as a conclusion regarding the over-all response of Subject 4). The section on "Methods" includes some, but not all, details concerning the special diet, as well as reference to the results of the study. In conclusion, this paper is a highly provocative study whose significance is obscured by incomplete and disjunctive reporting.

PARSONS, Montrose, N. Y.

SUBARACHNOID ALCOHOL BLOCK IN THE MANAGEMENT OF PAIN IN MALIGNANT DISEASE. D. M. PERESE, A. M. A. Arch. Surg. 76:347 (March) 1958.

Subarachnoid alcohol injection holds a definite place in the management of pain caused by malignant disease. It carries, however, some risk of complications and affords relief only over a limited period. The author has performed 148 alcohol blocks on 95 patients. Some of the patients required multiple injections, mainly to abolish bilateral pain. Alcohol injections can relatively safely be given at all levels, from the high cervical to the low lumbar region, provided a painstaking technique is observed (which is described in some detail). Of the 95 patients, 57 had complete relief from two weeks to over one year; 32 had partial relief, and 6 were not helped at all. Serious complications, such as paresis of the legs or urinary incontinence, occurred in 14% of the cases; yet these undesirable side-effects were only temporary in some instances. Subarachnoid alcohol block is specifically indicated when life expectancy is short and the patient is in poor condition.

LIST, Grand Rapids, Mich.

CONSERVATIVE THERAPY IN PERIPHERAL NERVE DYSFUNCTION. K. C. KEELER, J. A. M. A. 162: 1596 (Dec. 29) 1956.

When a peripheral nerve is injured, it attempts to regenerate. The management of a peripheral nerve injury consists of providing the most favorable conditions for return of function. Assuming that the etiology of the peripheral nerve dysfunction is known, management of the denervated motor elements and joints during the period of absent voluntary function must be based on pathophysiological conditions. The treatment of peripheral nerve dysfunction is here illustrated by a detailed description of the physical therapy applied in a case of neuropathy of the facial nerve and in peripheral nerve dysfunction in an extremity. The aim is to stimulate the contracted elements of muscle temporarily denervated, retain extensibility of fibrous tissues in and about the muscle, maintain elasticity of the capsule about affected joints, promote increased blood supply, and insure good position and motion of the affected part during the recovery period. Electrical stimulation, passive motion, assistive exercises, and dynamic bracing are important. Electromyography gives valuable information and can be used to motivate the patient. Exercise, to be effective, should be against sufficient resistance and should continue until the parts involved have regained strength in proportion to the demands of the patient's occupation.

ALPERS, Philadelphia.

ISONIAZID IN TREATMENT OF MULTIPLE SCLEROSIS: REPORT ON VETERANS ADMINISTRATION COOPERATIVE STUDY. VETERANS ADMINISTRATION MULTIPLE SCLEROSIS STUDY GROUP, J. A. M. A. 163:168 (Jan. 19) 1957.

Isoniazid, given three times daily in 100 mg. capsules, was compared with a placebo as to its effects on patients with multiple sclerosis. Special efforts were made to verify the diagnosis, avoid unnecessary risks to the patient, extend the period of observation sufficiently to provide a real test, include enough patients in whom the disease had recently been active, and eliminate bias through randomization and double-blind procedures. The 186 patients finally selected were enrolled in 11 hospitals; 88 received isoniazid, and 98 received the placebo. In evaluating the

results, each patient was rated as to the severity of his symptoms before and after the period of medication according to the modified Kurtzke scale. The patient was also rated as to a variety of specific neurological changes, self-care score, and ambulation score. By all criteria, including laboratory findings and over-all clinical impressions, the differences between the isoniazid and the placebo group were insignificant. No beneficial effects that could be ascribed to isoniazid in multiple sclerosis were observed in nine months or more of follow-up study.

ALPERS, Philadelphia.

ISONIAZID IN TREATMENT OF MULTIPLE SCLEROSIS. J. F. KURTZKE and L. BERLIN, J. A. M. A. 163:172 (Jan. 19) 1957.

In a preliminary report by Kurtzke and Berlin on the effects of isoniazid in treatment of multiple sclerosis, the course of 30 hospitalized patients given this agent over the preceding years was presented. Some 90% of these patients had improved while receiving isoniazid. In the present report they relate their further experiences, including 35 additional patients. The authors found that the clinical results of therapy with isoniazid for multiple sclerosis, while effecting subjective and objective improvement in a large percentage of cases, cannot be considered significant. New exacerbations continued to occur whether or not isoniazid therapy was continued.

ALPERS, Philadelphia.

THERAPEUTIC PROBLEMS IN DIABETES INSIPIDUS. E. C. CLARK and R. V. RANDALL, J. A. M. A. 163:341 (Feb. 2) 1957.

Clark and Randall point out that a triphasic curve of fluid exchange and specific gravity may occur during the onset of diabetes insipidus in both experimental animals and human beings. Recognition of the three phases of water metabolism, namely, (*a*) the transient stage, (*b*) the interphase, and (*c*) the permanent phase, during the development of this disorder raises certain therapeutic questions. In the first case described in this report, surgery in the vicinity of the optic chiasm was followed (*a*) by a polyuria of 27,930 cc. in 24 hours, then (*b*) by a gradual return to normal urinary output at about the sixth day, and finally, after about three days of normal output, (*c*) by establishment of a permanent phase of diabetes insipidus amenable to treatment with vasopressin tannate. Animal experiments suggest that the interphase (*b*) can be explained as meaning a transient outpouring of antidiuretic hormone by the detached, degenerating posterior lobe. The permanent phase (*c*) then represents exhaustion of the antidiuretic material from the posterior lobe. Severe diabetes insipidus is known to occur only in the presence of a functioning anterior pituitary lobe. In the third case here described, a polyuria had existed for a more than six years in the presence of signs of hypophyseal disease. A spontaneous amelioration of the polyuria was then noted concurrently with signs that the anterior lobe was failing; the polyuria returned after treatment with cortisone was begun. Spontaneous remission in a long-standing case of diabetes insipidus should alert the clinician to the possibility that the anterior lobe of the hypophysis is becoming involved in the disease process.

ALPERS, Philadelphia.

PRESENT STATUS OF ULTRASOUND IN MEDICINE. F. FRIEDLAND, J. A. M. A. 163:709 (March 9) 1957.

Friedland reviews the literature to present the highlights in the use of ultrasound in medicine. From present knowledge it appears that ultrasound is applicable to medicine in the following areas: 1. In the biophysical laboratory ultrasound as an investigative tool seems to have considerable applicability. 2. In physical therapy there is sufficient evidence on hand that ultrasonic therapy in nondestructive doses is a welcome addition for the relief of painful conditions of the neuromuscular and skeletomuscular system. 3. In the treatment of tumors, the use of ultrasound in destructive doses is still experimental. At present, however, it seems more than doubtful whether it will ever play a major role in this field. . . . Fragmentation of calculi has been done experimentally only. Destruction of bacilli has been demonstrated only in vitro. 4. In its diagnostic application for human diseases, ultrasound has shown promise, especially as far as the visual demonstration of soft tissues, pathological or normal, is concerned.

ALPERS, Philadelphia.

MANAGEMENT OF INTRACRANIAL BLEEDING. M. SILVER, J. A. M. A. 163:1097 (March 30) 1957.

Silver analyzes the findings, treatment, and results in 100 consecutive patients with intracranial bleeding. In every single case cerebral angiography was performed. A vascular malformation was demonstrated in 69%. A positive diagnosis as to cause or associated manifestation was made in 85%. While there are certain inherent risks in angiography, the author points out that no additional complications appear to have been introduced into the treatment of intracranial bleeding by having performed the procedure, even as early as two hours after the presumed onset of the bleeding. Such risks as may exist seem minor in comparison with the existing risk of the lesion itself. In cases of ruptured aneurysm of the circle of Willis, the survival rate following surgical intervention was 75%. In a smaller, but comparable, group, those treated by conservative means had a survival rate of 18%. Indicated surgical intervention is actually the conservative therapy for intracranial bleeding.

ALPERS, Philadelphia.

TREATMENT OF HEADACHE. A. P. FRIEDMAN and H. H. MERRITT, J. A. M. A. 163:1111 (March 30) 1957.

Friedman and Merritt evaluated over 5,000 patients having the symptom of chronic headache for their therapeutic response to various drugs (e. g., analgesics, sedatives, stimulants, antihistaminics, vitamins, and hormones). At present, the best method of drug evaluation is the use of the double-blind technique, in which a placebo and two or more therapeutic agents are administered to a group of untrained subjects. Relief of the symptoms of an acute attack of migraine can usually be obtained by the administration of ergot derivatives, particularly with a combination of ergotamine tartrate and caffeine. Phophylactic treatment of migraine with drugs alone does not yield satisfactory results. The best results in the treatment of tension headache are obtained by the use of a combination of analgesic and sedative drugs. The results obtained in the prophylactic therapy of tension headache with drugs were remarkably similar regardless of the form of therapy. Headaches associated with hypertension responded favorably to drug therapy for short periods of time, but the beneficial effects were only rarely maintained for more than a few months. The selection of suitable therapy for the treatment of headaches depends on the correct diagnosis, which includes the associated emotional tension and anxiety.

ALPERS, Philadelphia.

TREATMENT OF PARALYSIS AGITANS WITH ORPHENADRINE (DISIPAL) HYDROCHLORIDE: RESULTS IN 176 CASES. L. J. DOSHAY and K. CONSTABLE, J. A. M. A. 163:1352 (April 13) 1957.

Doshay and Constable gave orphenadrine in doses generally of 50 mg. three times daily to 176 patients with paralysis agitans. It was found to be compatible, and at times synergistic, with current anti-Parkinsonism agents, so that no changes in the previously established regimens of the patients were necessary. It brought some mitigation of symptoms to 98 of these patients, with striking benefits in some. There was relief of objective symptoms, such as sialorrhae, diaphoresis, oculogyria, and blepharospasm, with reduction of rigidity and tremor. In addition, subjective complaints of weakness, fatigue, and depression were frequently relieved by a marked euphoriant, energizing effect. Side-effects were few and were obviated by reducing the dosage. It was least effective in patients in whom major tremor was the dominant symptom, and the percentage of patients showing improvement was somewhat higher in the postencephalitic group than in the idiopathic and arteriosclerotic groups.

ALPERS, Philadelphia.

MANAGEMENT OF MYOFASCIAL PAIN SYNDROMES IN GENERAL PRACTICE. J. J. BONICA, J. A. M. A. 164:732 (June 15) 1957.

Bonica reviews the etiology, symptomatology, and methods of management of myofascial pain syndromes with trigger mechanisms. Myofascial pain syndromes are among the commonest causes of pain and disability, especially around the shoulders, low back, and neck. These disorders are usually the result of acute or chronic injury and are characterized by the presence of trigger areas and symptom complexes, which have definite patterns. Once these patterns have been learned, the sources of pain can be readily predicted. These conditions can be effectively treated with local block techniques in the form of infiltration with local anesthetic agents or application of ethyl chloride spray. The utility of this method is based on the assumption that in these disorders there is a self-sustaining cycle of pain-

spasm-pain persisting after the precipitating cause has disappeared; this cycle may be permanently abolished by interruption of the reflex mechanisms. In addition, physical therapy, corrective exercise, psychotherapy, and elimination of the predisposing and precipitating factors to prevent recurrences can all contribute to a cure, and the relief is sometimes dramatic.

ALPERS, Philadelphia.

IMPACT OF ISONIAZID ON TUBERCULOUS MENINGITIS. W. WEISS, G. M. EISENBERG, and H. F. FLIPPIN, J. A. M. A. 164:947 (June 29) 1957.

Weiss and his co-workers surveyed the case histories of 192 patients with tuberculous meningitis from 1943 to 1955. During the era preceding the introduction of specific therapy, in 1948, not a single one of 42 patients survived. During the subsequent five years, the era of streptomycin and aminosalicylic acid, the mortality rate was 84% in a group of 79 patients. After the introduction of isoniazid in 1953, the mortality fell to 54% in a group of 71 patients. The mortality has been lowest in patients under 41 years of age and was only 19% in a group of 16 patients less than 11 years old. No evidence was found to justify the continued use of the intrathecal route of administering streptomycin. Patients in whom the meningitis is accompanied by miliary tuberculosis have done as well, since the introduction of isoniazid, as those without miliary tuberculosis.

ALPERS, Philadelphia.

RELIEF OF JUVENILE INVOLUNTARY MOVEMENT DISORDERS BY CHEMOPALLIDECTOMY. I. S. COOPER, J. A. M. A. 164:1297 (July 20) 1957.

Cooper carried out a pilot study, during which chemopallidectomy was performed in 30 patients with various juvenile movement disorders. Among these were patients with choreoathetosis, rigidity, dystonia musculorum deformans, and hemiballismus.

Of the 30 patients subjected to operation, alleviation of involuntary movements was obtained in 20. There was one postoperative death, and one case was complicated by development of hemiparesis. Eight patients, in addition to the two in whom there were surgical complications, were not benefited by operation.

Chemopallidectomy is aimed only at the relief of hyperkinetic or involuntary movement disorders, and it will not relieve other abnormalities that are so frequently noted in congenital brain lesions.

ALPERS, Philadelphia.

TREATMENT OF MYASTHENIA GRAVIS. R. S. SCHWAB, K. E. OSSERMAN, and J. E. TETHER, J. A. M. A. 165:671 (Oct. 12) 1957.

Schwab and his co-workers used prolonged-action or slow-release tablets of neostigmine bromide, containing three regular doses of 15 mg. each, and a half-strength form, containing three doses of 7.5 mg. each, in the treatment of a series of 85 patients with myasthenia gravis. At the end of the experimental study it was noted that 54 of the 85 patients found them superior to their regular medication and are still taking them. Prolonged-action or slow-release tablets of pyridostigmine (Mestinon) bromide, containing three regular doses of 60 mg. each, and half-strength form, containing three doses of 30 mg. each, were tried in treating 109 patients with myasthenia gravis. Of this series, 82 of the 109 patients still continue to take the tablets. The average duration of action of the slow-release pyridostigmine tablet was approximately six hours. There were many individual differences in the responses to these dosage forms, and some patients preferred to take the slow-release tablets only at bedtime. Their greatest value was in eliminating the need of frequent interruptions of sleep.

ALPERS, Philadelphia.

EVALUATION AND MANAGEMENT OF THE BRAIN-DAMAGED PATIENT. J. S. TOBIS, M. LOWENTHAL, and S. MARINGER, J. A. M. A. 165:2035 (Dec. 21) 1957.

Tobis and his colleagues present this review as a guide to the physician in evaluating more critically the spectrum of disabilities of brain-damaged patients, and thereby to extend these patients' capacity to function more effectively. Rehabilitation of the brain-damaged patient, as in all rehabilitation care, is directed to the symptomatology. This symptomatology is dependent upon the nature, extent, and location of the organic disease and affects the performance of the musculoskeletal system (walking, feeding, and dressing), and the mentation, mood, and personality, as demonstrated in communication and social attitudes. Brain function is dependent upon the organization of the sensory, motor, and associational systems.

The extent of disorganization in the brain-damaged patient determines the symptomatology and the basis for management. These workers emphasize that brain-damaged patients generally present involvement in all three spheres—namely, sensory, motor, and intellectual—although too often this condition has been regarded solely as disorganization of the mental sphere. It is pointed out that a system of therapy has been developed in the field of physical medicine and rehabilitation based on this uniformity of symptomatology. This field, in collaboration with those of neurology, psychiatry, and psychology, has a contribution to make in both the evaluation and the management of brain-damaged patients.

ALPERS, Philadelphia.

ANTICOAGULANT THERAPY IN CEREBRAL VASCULAR DISEASE—CURRENT STATUS. C. H. MILLIKAN and J. P. WHISNANT, J. A. M. A. 166:587 (Feb. 8) 1958.

The prevention of thrombosis in cerebral vessels by the administration of anticoagulant drugs is the subject of this study. The word "prevention" is emphasized, as the evidence is tenuous that anticoagulant can cause dissolution of a thrombus when it is well established and no evidence exists that anticoagulants have any beneficial action on infarcted brain. Millikan and Whisnant used anticoagulant therapy (heparin, ethyl biscoumacetate, and bishydroxycoumarin) in 317 patients with manifestations of cerebral vascular disease. A group of 94 patients were classified as having intermittent insufficiency in the vertebral-basilar system, and in 90 of these the attacks stopped completely soon after the anticoagulant effect of the drugs became demonstrable by laboratory tests. A group of 107 patients with irreversible vertebral-basilar thrombosis had a mortality rate of only 8% on anticoagulant therapy, as compared with a rate of 58% reported for 31 similar patients who did not receive anticoagulants. A group of 85 patients with intermittent insufficiency in the carotid system were treated with anticoagulants, and in 82 the characteristic attacks were stopped. Of a group of 31 patients actively advancing carotid thrombosis went on to hemiplegia in only 6%, as compared with 55% of a reported series of 17 similar patients who did not receive anticoagulants. The authors point out that anticoagulant treatment is preventive, rather than reconstructive, but does act favorably on the natural history of cerebral vascular disease in patients of these four types.

ALPERS, Philadelphia.

USE OF ANTICOAGULANTS IN TREATMENT OF CEREBRAL VASCULAR DISEASE. E. MCDEVITT, S. A. CARTER, B. W. GATSE, W. T. FOLEY, and I. S. WRIGHT, J. A. M. A. 166:592 (Feb. 8) 1958.

McDevitt and her co-workers studied the long-term effects of anticoagulant therapy in 100 patients with evidence of cerebral vascular thrombosis or embolism. During 2,842 patient-months without anticoagulant therapy there were 229 thromboembolic episodes (67 being cerebral), as compared with 20 thromboembolic episodes (5 being cerebral) that occurred during 2,291 patient-months on anticoagulant therapy. Similar data permitted comparison of continuous with interrupted anticoagulant therapy, and it was found that 48 thromboembolic episodes occurred during 1,311 patient-months on interrupted therapy, as compared with 15 episodes during 957 patient-months on continuous therapy. The doses of anticoagulant (usually bishydroxycoumarin) were aimed to keep the prothrombin time for the undiluted plasma between 20 and 40 seconds. Hemorrhagic complications occurred in 30 of the 100 patients. There were 3 fatal cerebral hemorrhages, occurring over a period of 2,532 patient-months of anticoagulant therapy. The authors interpret these results to mean that anticoagulant therapy is effective in reducing the danger of recurrent thromboembolic episodes if contraindications are observed and prothrombin times are painstakingly controlled.

ALPERS, Philadelphia.

DELIRIUM TREMENS. F. A. FIGURELLI, J. A. M. A. 166:747 (Feb. 15) 1958.

Figurelli treated 180 patients for fully developed delirium tremens. All were actively drinking on admission. Of these, 96% were admitted in delirium, and 4% went into delirium 1 to 48 hours later. This fact conflicts with the teaching that delirium tremens is a withdrawal syndrome.

The first 44 patients admitted were treated by conventional methods. The duration of the delirium averaged about seven days, and that of hospitalization, from two weeks to one month. The death rate with conventional treatment was 10%. From March 16, 1956, on, treatment of uncomplicated cases consisted of the complete withdrawal of alcohol and the

administration of promazine hydrochloride. Experience led to a program consisting of an initial intramuscular injection of 200 or 300 mg., a second injection of 100 mg. within four hours or less, and oral administration of 100 mg. four times a day for maintenance thereafter. A large percentage of the patients in this series recovered from delirium tremens in the first 24 hours, and the great majority, in 48 hours. The over-all mortality with promazine treatment, both oral and parenteral, and in all doses, was 4.5%. In the last 87 cases there were no deaths. The prompt control of delirium and the lowered mortality in the promazine-treated cases contrast sharply with the prolonged illness and higher mortality associated with older methods of treatment.

ALPERS, Philadelphia.

FECAL INCONTINENCE—NONSURGICAL TREATMENT. R. J. JACKMAN, J. A. M. A. 166:1281 (March 15) 1958.

In the treatment of fecal incontinence, nonsurgical measures are often as important as the surgical, and in patients whose incontinence is neurogenic, as in paraplegia, only nonsurgical treatment can help. In discussing the mechanism of intestinal continence, Jackman points out that continence is maintained not so much by tonically contracted states of the internal or external sphincter of the anus as by reflex contractions of the external sphincter, initiated in the rectum. An additional neuromuscular mechanism, described as reservoir continence, resides in the descending colon. Nonsurgical measures for fecal incontinence fall into five phases: (1) diet, of a low-residue type; (2) drugs, including those that decrease intestinal peristalsis and those that tend to "soak up" water from the intestine, thus giving more form to the stool; (3) irrigation of the lower part of the intestine, especially when seepage or leakage throughout the day is a problem; (4) exercise for the anal muscles, and (5) psychotherapy. These measures may be used singly or in combination, as each patient's particular problem dictates.

ALPERS, Philadelphia.

PROGNOSIS AND TREATMENT OF MULTIPLE SCLEROSIS—QUANTITATIVE NOSOMETRIC STUDY. L. ALEXANDER, A. W. BERKELEY, and A. M. ALEXANDER, J. A. M. A. 166:1943 (April 19) 1958.

Alexander and his co-workers used as the basis for this study repeated quantitatively scored neurological examinations. A total of 5,635 such examinations were carried out on 554 patients with multiple sclerosis. Observations extended up to eight years. The general course of the illness was studied for all patients, as well as for specific subgroups distinguished by sex and age at onset of disease and by inclusion in various treatment and control groups. The authors present evidence that a severe and a mild form of the disease exist, although there is some overlap of these two groups. On the basis of their quantitative method, the severe and mild cases can be distinguished from the sixth year of the disease onward, since the relatively most active progression of the disease takes place during the first five years. Evaluation of treatment, therefore, requires comparison with carefully matched controls. Studied in this way, the only treatments showing an objective quantitative effect on the course of the disease were repeated blood transfusions and corticotropin therapy. Blood transfusions have their place in the treatment of early and relatively mild cases in patients who have infrequent attacks and are without progression of disability due to scar formation in the intervals between attacks. Corticotropin therapy is the treatment of choice at the time of the full-blown, moderate to severe development of the disease, when attacks are relatively frequent and progression of the disease continues during the intervals.

ALPERS, Philadelphia.

ACTH AND CORTISONE IN GUILLAIN-BARRÉ SYNDROME: REVIEW OF THE LITERATURE AND REPORT OF A TREATED CASE FOLLOWING PRIMARY ATYPICAL PNEUMONIA. F. J. BERLACHER and R. B. ABINGTON, Ann. Int. Med. 48:1106 (May) 1958.

Berlacher and Abington review the literature of 25 cases of the Guillain-Barré syndrome treated with corticotropin and cortisone. The rationale for such therapy stems from the possible allergic etiology of the process. The patients are classified under three groups: (1) those in whom the neurologic disease was still progressive, (2) those in whom the neurologic disease was stationary, and (3) those in convalescence.

From the data compiled, it was found that 87.5% of the 16 patients in Group 1 had arrest of the disease upon institution of adequate therapy. Only two of the six patients in the

second group showed improvement. None of the three patients in the third group improved.

Therapy consisted of the usual cortisone and corticotropin dosages continued for two to four weeks, with gradual reduction. If there was no response within the first week, nothing was to be gained by continuing the drug administration.

The authors report a case with proved primary atypical pneumonia complicated by the Guillain-Barré syndrome, with successful response to cortisone therapy.

AIGNER, Rochester, Minn.

THE ADVANTAGES OF OPENING CERTAIN INTRACRANIAL ANEURYSMS. J. R. GIBBS, J. Neurol Neurosurg. & Psychiat. 20:165 (Aug.) 1957.

Of the many techniques available in the treatment of intracranial aneurysm, none is universally available to a particular type of case. Gibbs reports three cases of intracranial aneurysm—two on the middle cerebral artery and one on the internal carotid artery in the cavernous sinus. In the latter case, herniotomy was performed for therapeutic, rather than technical, reasons, in order to relieve severe facial pain caused by compression of internal carotid aneurysm. In the two middle cerebral artery aneurysms, herniotomy was performed when the sac was so large and thin-walled that it could not be safely retracted to afford a proper view of its origin, or an anatomical arrangement was discovered at the neck of the aneurysm which would endanger the potency of the parent vessel when clipped or ligated.

MANDEL, Philadelphia.

PATHO-ANATOMIC AND HISTOPATHOLOGIC CHARACTER OF LESIONS IN THE CENTRAL NERVOUS SYSTEM IN MAN FOLLOWING ANTI-RABITIC TREATMENT. E. JONES, J. Neuropath. & Exper. Neurol. 17:315 (April) 1958.

Jones reports the case of a 56-year-old farmer who handled, but was not bitten by, a rabid dog and was treated with anti-rabies vaccine. He became acutely ill after this and died in four months. Autopsy showed firm or spongy circumscribed lesions in the temporal and frontal lobes. Microscopically, there were large lesions in the brain and spinal cord which were perivascular and well demarcated, with definite advancing walls and a less intensely stained central zone. The incidence of neuroparalytic accidents, as reported in the literature, varies from 0.028% to 0.77% in rabies-vaccine-treated patients. Of these patients, many recover. The fatality is 0.005% to 0.007%. Two-thirds develop during the course of treatment and one-third after its completion. The changes can be divided into three clinical groups: (1) acute ascending paralysis (Landry's type); (2) thoracolumbar myelitis, and (3) peripheral neuritis. The mortality varies from 30%, in the first group, to none, in the third. The CSF showed an increase of lymphocytes and polymorphonuclear cells up to 800 per cubic centimeter, with an increase in protein to 100 mg. % and a moderately abnormal colloidal gold curve.

Most of the cases reported had the characteristics of an acute disseminated sclerosis with marked demyelination. In 80% of patients who suffered neurologic complications from rabies prophylaxis, there was a history of other allergic disease. The author believes there is sufficient reason to assume that the lesions in the central nervous system following antirabic treatment are the result of an allergic response.

AIGNER, Rochester, Minn.

Encephalography, Ventriculography and Roentgenography

DIAGNOSIS AND TREATMENT OF EOSINOPHILIC GRANULOMA OF SKULL. R. S. KNIGHTON and J. DEW. FOX, J. A. M. A. 162:1294 (Dec. 1) 1956.

The diagnosis of eosinophilic granuloma of bone was made in five cases here reported. In each case there was a circumscribed area of swelling or tenderness on a cranial bone, a characteristic circumscribed lytic lesion in the roentgenograms, and confirmation by microscopic examination of tissue obtained at operation. Headache, attributable to extension of the tumor along meningeal blood vessels, was severe in one case and present in two others. The intracranial pressure was normal, and the neurological findings were negative in all cases. Surgical removal and subsequent irradiation, to a total of 600 to 2000 r in air, was followed by healing and complete relief of symptoms. The authors point out that eosinophilic granuloma should be considered as a diagnostic possibility whenever a patient presents localized tenderness of the scalp or a lytic lesion of the skull.

ALPERS, Philadelphia.

CERVICAL DISKOGRAPHY. R. B. CLOWARD, Am. J. Roentgenol. 79:563 (April) 1958.

Cloward describes the technique he uses in performing cervical discography and gives his impressions concerning the value of the procedure, based upon his experience with 41 patients for whom cervical discograms were obtained in a period of 18 months. With the patient in the position in which he will be kept for the procedure, anteroposterior and lateral roentgenograms of the cervical spine are exposed and developed. Morphine is used routinely before the procedure. Barbiturates also are used with apprehensive patients. The vertebral body in the region of the cervical spine to be studied is palpated with the finger tips of the operator, which have been placed in the groove between the carotid sheath and the trachea. The soft tissues in this region are anesthetized with procaine, including the periosteum of the anterior longitudinal ligaments. When anesthesia has been carried out thoroughly, it is possible to palpate the vertebral bodies with hard pressure and often to feel the humps made by the intervertebral discs. Cloward usually studies the disc spaces between C5 and C6 and between C6 and C7, since abnormal discs most frequently are found at these two interspaces. Palpation is continued with the index and middle fingers, which are pressed tightly against the anterior surface of the vertebral bodies. A 20-gauge needle, 2 in. (5 cm.) in length, is passed through the skin and soft tissues between the fingers until it reaches the disc. It is inserted 1 or 2 mm. through the anterior longitudinal ligament and the anterior fibers of the annulus fibrosus. The patient may not talk, cough, or swallow now, since to perform any of these functions would dislodge the needle from the disc. A lateral roentgenogram is exposed and developed to determine the position and direction of the needle. If the roentgenogram confirms the clinical impression that the needle point has penetrated the anterior surface of the correct intervertebral disc space, a fine needle is passed through the 20-gauge needle and into the nucleus pulposus. The fine needle is made only 1 cm. longer than the larger one, so that there is no danger of advancing it too far. Once again, the position of both needles is checked with lateral and anteroposterior roentgenograms. If these films show the position to be correct 0.1 to 0.2 cc. of 50% diatrizoate (Hypaque) sodium or 70% sodium acetrizoate (Urokon Sodium) injected through the small needle. The normal nucleus pulposus of a cervical disc will accept only 0.2 to 0.3 cc. of solution; so a concentrated medium must be used. Thirty-five per cent iodopyracet (Diodrast) in this quantity is not roentgenographically visible. Once again, anteroposterior and lateral roentgenograms are made with the needles in position. If the films are not satisfactory, additional opaque solution can be injected. If the films are satisfactory, the needles are removed, and an additional set of films are taken without the needles in place. There are three types of pathologic cervical discs which may cause clinical symptoms. The first type is the so-called "soft disc." This can be found with recent whiplash injuries and presents no specific abnormal findings in plain films of the spine. Loss of the normal curvature, of course, may be present, but there is no narrowing of the intervertebral disc space and no evidence of hypertrophic change about its margin. The second type of abnormal cervical intervertebral disc which may cause symptoms is the degenerated disc of long standing. Such discs are easily demonstrated in the plain roentgenograms of the spine by narrowing of the intervertebral disc space and proliferation of hypertrophic bone around the margins of the disc space. The third type of abnormal cervical intervertebral disc producing symptoms is massive disc protrusion into the spinal canal. These lesions are often diagnosed as tumors and often show obstruction of the spinal canal when myelograms are performed. The differentiation between tumor and a large herniated disc can be demonstrated easily if the involved disc can be injected successfully. Cloward concludes that the procedure of cervical discography is relatively simple and safe. It has diagnostic advantages over cervical myelography. He hopes that it may be useful in the differential diagnosis of symptoms relating to the cervical cord and nerve roots, many of which can be caused by protrusions of the cervical intervertebral discs.

WEILAND, Grove City, Pa.

PRIMARY RETICULUM CELL SARCOMA OF THE SKULL. D. P. ULLRICH and P. C. BUCY, Am. J. Roentgenol. 79:653 (April) 1958.

Three cases of primary reticulum-cell sarcoma of the skull previously have been reported in the medical literature. Ullrich and Bucy add a fourth case. The patient was a white woman aged 53. She had had advanced bilateral pulmonary tuberculosis, which had been treated by bilateral pneumothorax and a left thoracoplasty. However, roentgenograms of the chest had shown no change for a period of five years at the time the abnormality in her skull was discovered. The patient had been experiencing pains in the left occipital region and the left

frontal region of her head for eight months. In these regions of the skull there were areas which were tender to palpation. Serial roentgenograms of the skull made over a period of six months showed progressive bone destruction in the left frontal and left occipital regions. The bone lesions were thought likely to be caused by a low-grade osteomyelitis, probably tuberculous osteomyelitis. Both areas of involvement of the skull were removed surgically by separate operations. Pathologic examination of the removed tissue was interpreted as showing reticulum-cell sarcoma in both sites of the skull. There was no evidence of tuberculosis. A roentgenogram of the skull made six weeks after operation showed minimal marginal changes of erosion in both craniectomy sites. A general roentgenologic survey of the skeleton was made, but no other areas of neoplastic involvement of bone were found. Roentgen therapy was given to both craniectomy sites in the skull. A tumor dose estimated at between 3,500 and 4,000 r was given to each craniectomy site, using radiation with a half-value layer of 0.9 mm. Cu. The patient has been well for five years, without evidence of recurrence of the tumor in the skull or elsewhere. Strange and de Lorimier reported two cases of primary reticulum-cell sarcoma of the skull which were biopsied but were treated only with radiation. Both patients are alive and well—one nine and one three years after treatment. A third patient died after a period of two and a half years. Strange and de Lorimier suspected that the third patient might have had an undiscovered primary site elsewhere with metastasis to the skull. The prognosis of primary reticulum-cell sarcoma of the skull, when treated with radiation alone or with a combination of radiation and surgery, seems to be good, as judged by experience with this very small number of cases.

WEILAND, Grove City, Pa.

ROENTGENOGRAPHIC ABNORMALITIES IN SOLDIERS WITH LOW BACK PAIN: A COMPARATIVE STUDY, F. J. FISCHER, M. M. FRIEDMAN, and R. E. VAN DEMARK, Am. J. Roentgenol. 79:673 (April) 1958.

Twelve years ago these authors published an article describing the roentgenographic findings in a normal low back. At that time they made a detailed roentgenographic study of 100 soldiers who had never suffered an injury to the back and who had never had backache. The present study consists of similar roentgenographic views of the low back (lumbosacral spine) made on 200 male soldiers who presented themselves consecutively for treatment because of back pain at the lumbar and sacroiliac levels. Comparisons were made between the control group, studied 12 years ago, and the symptomatic group, studied recently. The following abnormalities were found in significant numbers in both groups: spina bifida occulta, transitional lumbosacral vertebrae, asymmetric facets, degenerative joint disease, spondylolisthesis, and increased acuity of the lumbosacral angle. Other abnormalities were found in smaller numbers. Lumbar spines showing no roentgen variations from normal were found in 20% of the control group in 20% of the symptomatic group. Most abnormalities demonstrated roentgenographically had approximately equal incidence in the two groups. Degenerative joint disease of the lumbosacral joint and sacroiliac joints, narrowing of the lumbosacral interspace, and increased acuity of the lumbosacral angle were found slightly more frequently in the symptomatic group, but the difference was not great. The only abnormality in which there seemed to be a large difference between the two groups was defect of the neural arch (spondylolysis and spondylolisthesis). Spondylolysis and spondylolisthesis together were found in 6% of the control group and in 14.5% of the symptomatic group. Thus, the incidence of these abnormalities was approximately two and one-half times as great in the symptomatic group of soldiers.

WEILAND, Grove City, Pa.

WHIPLASH INJURIES OF THE CERVICAL SPINE. D. B. NAGLE, Radiology 69:823 (Dec.) 1957.

Whiplash injuries and roentgen examinations for possible whiplash injuries are becoming much more frequent as the result of the increase in automobile accidents. A whiplash injury of the cervical spine consists of hyperflexion of the neck resulting from a sudden forceful forward thrust of the head when the motion of the body has been suddenly slowed or stopped. This type of a whiplash injury is seen with head-on collisions. A recoil-type hyperflexion is seen following injuries associated with sudden forward acceleration, as when an automobile is struck from behind. At first the patient's neck is hyperextended, and hyperflexion occurs as a recoil mechanism. These whiplash injuries may cause fractures of the bones, tearing of the ligaments, or straining of the muscles. The nature of some of the most serious injuries is obvious either from the clinical or from the roentgen examination. More difficulty is encountered in those patients who show no gross clinical sign of injury or who are suspected

of having an injury but show no abnormality on routine roentgenography. Having ruled out serious injury by anteroposterior and lateral films taken with the patient recumbent, one is justified in proceeding with a more extensive study. Erect lateral projections with the neck in neutral position, with the neck flexed, and with the neck extended are helpful. Oblique views may be the only views which show fractures of the posterior neural arch, pedicles, or joint facets. Laminagrams are helpful in demonstrating fractures of the odontoid process of details of the atlanto-occipital and atlantoaxial joints. When no fracture is present, tearing of ligaments can often be demonstrated by comparing the normal lateral view with the lateral view made in flexion. Such injuries usually begin as a tear of the capsular structures of the zygapophyseal joints, followed by rupture of the interspinous ligaments, and then tears of the fibers of the annulus fibrosus occur, with resulting disc injury. Views made with forced flexion of the neck will show wider-than-normal separation between the spinous processes of the two involved vertebrae. There may be some forward slipping of the one vertebra on the other, and the zygapophyseal joint spaces may be widened. These are localized changes, confined to the two vertebrae involved. Muscle strains without tearing of ligaments and without fracture usually produce muscle spasm with straightening, or even reversal, of the normal lordotic curvature in the cervical region and limitation of all motions. However, in such cases there is no focal disruption of the curvature and no focal malalignment of the bones, as we find with injuries to the ligaments.

WEILAND, Grove City, Pa.

MENINGIOMAS OF THE POSTERIOR CRANIAL FOSSA. T. A. TRISTAN and P. J. HODES, Radiology 70:1 (Jan.) 1958.

Sixty-four patients having meningiomas of the posterior cranial fossa were seen between the years 1918 and 1955 at the Graduate Hospital and the Hospital of the University of Pennsylvania in Philadelphia. Tristan and Hodes made a study of the hospital records of 59 of these 64 patients. Radiographs were available for review in only 26 cases, but radiologic interpretations were found on the other charts. Meningiomas of the posterior cranial fossa are difficult to diagnose but often are amenable to surgical removal if they can be diagnosed. In this series of cases about 1 in 12 of all meningiomas found in these hospitals occurred in the posterior cranial fossa. Gliomas are the commonest neoplasms occurring in the posterior fossa, acoustic neurinoma being the second most frequent tumor here, and the meningioma the third. The classification of Castellano and Ruggiero was used in this series of patients. This classification depends upon the site of origin of the meningioma. Meningiomas in Class I arise in the dura covering the inferior convex surface of the cerebellum. Of the 59 patients, 14 had tumors falling into this classification. The earliest symptoms of note with these tumors usually are those of increased intracranial pressure. More than half of the patients show cerebellar dysfunction and nystagmus. Plain roentgenograms of the skull may show evidence of increased pressure and may reveal psammomatous calcification in the tumor. Pneumoencephalograms may show internal hydrocephalus if the tumor is large enough to cause blockage of the fourth ventricle or the aqueduct of Sylvius. A significant sign of such a tumor is upward displacement of the posterior portion of the third ventricle by the tumor, together with anterior displacement of the aqueduct of Sylvius and the fourth ventricle. Vertebral angiograms may show upward displacement of the homolateral posterior cerebral and superior cerebellar arteries. Meningiomas arising from the tentorium cerebelli are grouped in Class II. They may lie in a totally infratentorial position or may grow through the tentorium and present both infratentorially and supratentorially. Diffuse headache is usually the predominant symptom in this group. Vomiting and vertigo are seen in over half the patients. Papilledema is the commonest objective sign. The roentgen findings are similar to those of Class I tumors. Eight of the fifty-nine tumors were of Class II. Meningiomas arising from the dura covering the posterior surface of the petrous portion of the temporal bone form Class III. These tumors are true cerebellopontine-angle tumors and are the commonest type of posterior-fossa meningioma. Twenty-eight of the series were found in Class III. Involvement of the eighth cranial nerve can be demonstrated in 80% to 100% of cases. Deafness and tinnitus, often of long duration, are the two commonest findings. Thus, the tumors cannot be distinguished clinically from acoustic neurinoma. Hodes previously reported a series of 183 patients with cerebellopontine-angle tumors, in which 10% of the tumors were found to be meningiomas. When a meningioma presents as a cerebellopontine-angle tumor, increased bone density is a little more commonly found than

bone erosion. Pneumoencephalograms are important in these patients, for rather typical findings have been described. There is an upward transtentorial herniation of the brain stem and cerebellum; the lateral ventricles, the third ventricle, and the proximal portion of the aqueduct are dilated, and usually the fourth ventricle is either not demonstrated or is shifted posteriorly. Vertebral arteriograms may show a "tumor stain" and may reveal some lateral or backward displacement of the basilar artery. Class IV of posterior-fossa meningiomas are those arising over the clivus. They are difficult to localize clinically. Cranial nerve disturbances are the most frequent findings. These meningiomas are inoperable. Only 2 of the 59 patients had meningiomas in this location. Class V consists of meningiomas of the foramen magnum, which also is a rather infrequent location. Only three of the series were found here. Pain in the occipital region of the neck is the commonest symptom. The symptoms of such tumors are usually vague, and there may be periods of remission of symptoms. These tumors can become fairly large before well-defined symptoms occur. Eventually a cranial-spinal syndrome occurs, with paresis of a hemidiaphragm, paralysis of extremities, hemianesthesia, etc. Routine radiographs of the head and spine usually show no abnormality. Cervical myelograms have been of limited value. Pneumoencephalograms are dangerous because of the hazard of herniation of the brain stem. When the diagnosis is suspected, a ventriculogram would seem to be preferable to a pneumoencephalogram; yet deaths have followed either procedure. The most helpful factor in diagnosing posterior-fossa meningiomas is a high index of suspicion. The complaints usually tend to be nonspecific, but often enough objective evidence can be amassed to make a diagnosis possible if the lesion is suspected by the clinician.

WEILAND, Grove City, Pa.

OBSERVATIONS ON THE 24-HOUR PNEUMOENCEPHALOGRAM WITH SPECIAL REFERENCE TO THE DIAGNOSIS OF CORTICAL ATROPHY. M. T. SCHNITKER and R. P. ULRICH, Radiology 70:15 (Jan.) 1958.

Schnitker and Ulrich took erect films of the skull 24 hours after pneumoencephalography had been performed on 66 patients whom they considered to have no progressive lesions of the brain. The original pneumoencephalograms were taken with the patient in the upright position, with air replacing fluid on a volume-for-volume basis, until the cerebrospinal system was emptied of fluid in most cases. In this series, 15 patients were less than 16 years old; 38 were between 16 and 60 years old, and 13 were over 60 years old. In 56 of the 66 cases the pneumoencephalograms were found to show definite evidence of subdural air in the 24-hour film. This constituted a percentage of 85% showing subdural air. The percentage was slightly higher for adults. The pneumoencephalograms were taken for three clinical reasons: suspected cerebral atrophy, post-traumatic syndrome, and ordinary headache. No tumors or gross abnormalities are included in the study. It has been thought that the presence of subdural air after pneumoencephalography either indicates a failure in technique in performing the study or is a result of previous trauma to the meninges. The presence of subdural air in such a large percentage of cases in patients such as these suggests that it is a normal finding, and that there is some normal manner for the air to get from the subarachnoid to the subdural space. Schnitker and Ulrich hypothesize that the air may pass by way of the projections of the Pacchionian granulation bodies, which cross the subdural space at the vertex of the skull, along the longitudinal sinus. The authors attempted to estimate the amount of subdural air which was present and to estimate the volume of the skull. They then expressed the amount of subdural air as a percentage of skull volume. A higher percentage of subdural air tended to be present in patients over 60 years of age. The percentage was considerably lower in patients under 16 years of age. It appears that cortical atrophy cannot be diagnosed accurately from estimations of the amount of subdural air found in the 24-hour film made after pneumoencephalography.

WEILAND, Grove City, Pa.

SMALL PNEUMOENCEPHALOGRAMS AS A SCREENING PROCEDURE IN THE STUDY OF CONVULSIVE DISORDERS. L. E. ETTER and E. L. YOUNGUE, Radiology 70:23 (Jan.) 1958.

Etter and Youngue perform pneumoencephalography, using about 20 cc. of air, as a screening procedure in studying patients admitted because of undiagnosed convulsive disorders. The study technically is easier than when larger amounts of air are introduced; the fourth ventricle is visualized more frequently with the smaller amount of air, and the unpleasant side-effects of the procedure are considerably reduced. Immediately after the injection of the air, erect anteroposterior and lateral views are taken and developed while the needle

is still in place. If these films show air in the lateral ventricles, a posteroanterior-oblique view for visualization of basal cisterns and the fourth ventricle is taken. The rest of the examination consists of recumbent views. Lateral views are made with the brow up and with the brow down and using a horizontal ray for visualization of the anterior and posterior horns of the lateral ventricles. Anteroposterior views are taken with a horizontal ray, first with the left side of the head down and then with the right side of the head down, in order to show the temporal horns. Posteroanterior and anteroposterior views are made with a vertical ray, and, finally, right lateral and left lateral views are made with a vertical ray. In some cases where abnormality is suggested the small pneumoencephalogram is followed after a few days by standard pneumoencephalography, in which larger amounts of air are used. This is done in order to obtain more detailed information concerning the suspected abnormality. The tabulated data by Etter and Youngue suggest that the pneumoencephalograms using a small amount of air show equal accuracy to the ones using large amounts of air, and far fewer of the small pneumoencephalograms are technically unsatisfactory.

WEILAND, Grove City, Pa.

NEUROFIBROMATOSIS AND INTRATHORACIC MENINGOCELE. C. J. LAVIELLE and D. A. CAMPBELL, Radiology 70:62 (Jan.) 1958.

LaVielle and Campbell report the case of a 36-year-old woman who showed skin changes typical of von Recklinghausen's neurofibromatosis and who was studied because of pain in the low thoracic region. A large mass was found in the posterior portion of the right hemithorax. The mass had caused dislocation of the right 11th rib and bone erosion of the pedicles and the posterior margins of the bodies of the 11th and 12th thoracic vertebrae. Surgical exploration revealed the mass to be a large meningocele, communicating with the spinal canal. A chest film after operation showed a similarly located, but smaller, mass in the left hemithorax which was not suspected before operation and which later was proved to be another meningocele, because the opaque medium flowed into it during myelographic examination. Intrathoracic meningocele is a relatively uncommon entity. More than two-thirds of all reported cases have been associated with cutaneous neurofibromatosis. There are numerous theories concerning the cause of the abnormality. LaVielle and Campbell believe that congenital abnormalities of the mesoderm are the basic cause of these meningoceles. They believe that a weakened or abnormal area of bone or dura sets up conditions for their occurrence and that variations in spinal fluid and intrathoracic pressures may induce the herniation.

WEILAND, Grove City, Pa.

CYSTIC DEGENERATION IN GLIOBLASTOMA MULTIFORME: TRAPPED-AIR SIGN. G. S. LODWICK, Radiology 70:74 (Jan.) 1958.

While a Fellow in the Registry of Radiologic Pathology of the Armed Forces Institute of Pathology, Lodwick reviewed roentgenograms on 500 proved cases of primary tumors of the brain and spinal cord. In three cases of glioblastoma multiforme he noticed multiple radiolucencies within the brain substance in ventriculographic films. He interpreted these as representing bubbles of gas within the brain substance. He has observed this sign in three additional cases since that time. Glioblastoma multiforme is a rapidly growing tumor which becomes necrotic centrally and forms fluid-filled cysts, which intercommunicate. If the tumor is so situated that the needle passes through the tumor during the process of performing ventriculography, a communication may be established between the ventricular system and the fluid-filled cysts of the tumor. In such cases air can displace the fluid in some of the cysts and produce the trapped-air sign which Lodwick describes. This sign will not be found with most glioblastomata, for it is probable that the needle will not pass through most of them. In addition, there are a number of other pathologic conditions of the brain in which fluid-filled cysts can exist within the brain substance and thus can show air in a ventriculogram by the same mechanism as the glioblastoma. Such lesions as gliomas, hemangioblastomas, teratoid tumors, brain abscesses, porencephalic cysts, etc., might reasonably be expected to show this sign occasionally. Thus, the finding is not specific for glioblastoma multiforme, but the presence of multiple small cystic areas outlined by air can prove helpful in localizing the tumor and giving a clue concerning its nature.

WEILAND, Grove City, Pa.

THE MYELOGRAPHIC EXAMINATION OF THE FORAMEN MAGNUM. L. I. MALIS, Radiology 70:196 (Feb.) 1958.

Malis describes in detail a technique by which he has been successful in examining the region of the foramen magnum, with consistently good results. In cervical myelography the study often is stopped short of the foramen magnum, and lesions at this high level are frequently missed by the ordinary myelographic procedure. Malis uses about 12 cc. of iodophendylate (Pantopaque), injected into the lumbar region of the spinal canal, although he does not hesitate to increase the amount to 18 cc. or more if it is felt necessary. The patient is placed on the abdomen, as for a lumbar myelogram; the head is held in hyperextension, and the table is tilted sufficiently to permit the oil to run over the thoracic "hump" and into the cervical region. Extension of the head is necessary to keep the oil out of the head. Once the oil has entered the cervical canal, the table is returned to the horizontal position, and tilts thereafter are limited to small amounts in either direction. Flexion and extension of the head on the neck and of the neck on the shoulders are two different processes and can be kept independent of each other, although the patient must be taught this difference. Flexion of the neck with extension of the head is the maneuver that runs the oil into the region of the foramen magnum. The head is kept in such a position that the clivus is slightly higher than the anterior margin of the foramen magnum, thus preventing the oil from running up over the clivus, past the posterior clinoid processes, and into the anterior and middle cranial fossae. It is necessary to run the oil up over the clivus to the region of the posterior clinoid processes for complete examination, but oil run beyond this point is usually lost in the head and cannot be returned to the lumbar region. Malis utilizes ordinary anteroposterior spot films taken with the patient in the prone position and also utilizes "cross-table laterals," lateral views made with a horizontal x-ray beam traveling through the head and neck laterally and recording its image on a grid-front cassette propped up on the table edge. It is necessary to run the oil up the clivus far enough to identify the basilar artery in order to be sure that the region of the foramen magnum has been examined adequately. Malis feels that the danger of losing the iodopyracet in the ventricular system of the brain has been greatly exaggerated. Aside from an occasional headache after the procedure, little harm comes from such loss. However, by observing good technique and not rotating the head on the cervical spine, loss of the oil in the ventricles and cerebral cisterns can be avoided in most cases. The key to technical success with the method depends upon the proper manipulation of the head and neck. The examination would be contraindicated in patients for whom such manipulation would be dangerous.

WEILAND, Grove City, Pa.

EROSIVE RIB LESIONS IN PARALYTIC POLIOMYELITIS. C. BERNSTEIN, W. D. LOESER, and L. E. MANNING, Radiology 70:368 (March) 1958.

Bernstein, Loeser, and Manning studied serial chest x-rays on 28 patients with paralytic poliomyelitis representing successive admissions for treatment in a respirator center. The authors describe a peculiar erosion of the superior cortex of the posterior portion of the ribs, which apparently has not previously been described. It was found in 14 of the 28 patients. The lesion consisted at first of mild erosion of the superior cortex of a rib and showed continuous progression of the erosion in all cases studied. No cases showed rib regeneration. In the severest involvement there was almost total disappearance of bone structure throughout the area of the lesion, which may extend as far as 4 cm. along the course of the rib. The distribution of the lesions is usually symmetrical, and the third rib is the one involved in most cases. In 10 of the 14 positive cases there was symmetrical bilateral involvement of the third rib. When this lesion is found, the other ribs appear normal, and no unusual osteoporosis is found in the thoracic cage. The lesions do not produce symptoms. Biopsy was not mentioned in the article. The changes described in the ribs were not seen in any patient earlier than 10 months after the onset of paralysis, were usually seen after 20 months, and in one case did not appear until 45 months after the onset of paralysis. The lesions seemed to be unrelated to age, sex, type of therapy, or presence of decubitus ulcer. However, more severely paralyzed patients showed a greater frequency of incidence. The authors advance the theory that the lesions may be caused by continued pressure of the medial margin of the scapula against the posterior aspect of the ribs.

WEILAND, Grove City, Pa.

CEREBRAL ANGIOGRAPHY WITH MIOKON. W. A. SHAFER and C. B. LECHNER, Radiology 70:557 (April) 1958.

Shafer and Lechner have used a 30% solution of sodium diprotrizoate (Miokon Sodium) in a series of 50 cerebral angiograms. In this series of cases they have encountered no untoward reactions or serious complications. The patients have been conscious throughout all of the procedures. The angiograms have been obtained by percutaneous injection, using only analgesic premedication and local anesthesia. Most patients have been aware only of a sensation of mild warmth on the side of the injection. The flushing, dilatation of the pupils, and subsequent neurological changes which have occurred with other opaque media have not been found with sodium diprotrizoate in this concentration. A few patients who had previously undergone the same type of examination when a different contrast medium was used have commented that the second examination was much less disturbing than the first. Ten cubic centimeters of the medium has been injected to obtain a series of lateral views. Then another 10 cc. has been injected to obtain a series of anteroposterior views. In most cases this amount of the contrast medium has proved to be sufficient, and the quality of the films has been excellent. The cerebral blood vessels appear a little larger in diameter than they do when other contrast media are used. This is thought by Shafer and Lechner to be the result of less irritation to the vascular tree. Since the examination is less bothersome to the patient, the patient is not likely to move during the exposure of films. This allows a longer exposure time to be chosen. The combination of longer exposure time, wider diameters of the arteries, and the high iodine content of the opaque medium all make for better visualization of the cerebral arterial tree. Capillary and venous filling seems as good as, but no better than, is found when other media are used. Shafer and Lechner conclude that cerebral angiography with sodium diprotrizoate is a safe and extremely valuable diagnostic procedure that should command a wider use.

WEILAND, Grove City, Pa.

IMPORTANT ASPECTS IN THE ROENTGEN STUDY OF THE NORMAL LUMBOSACRAL SPINE. I. MESCHAN and R. M. F. FARRER-MESCHAN, Radiology 70:637 (May) 1958.

The vertebral column develops embryonically in three stages: the membranous, the cartilaginous, and the ossific. The membranous stage of the human vertebral column develops before the fourth week of fetal life. Mesodermal segments, called sclerotomes, migrate to lie in paired segmental masses alongside the notochord. About the fourth week of fetal life two cartilaginous centers appear on either side of the notochord and rapidly extend around it, forming the bodies of the cartilaginous vertebrae. The neural arch of each vertebra then is formed in cartilage. During the cartilaginous stage of development the notochord is progressively compressed into the central regions of the intervertebral discs. Around the sixth week of fetal life three ossification centers appear in the cartilage, one for the vertebral body and one for each side of the neural arch. The rami of the lumbar neural arches unite during the first year of life. Union of the laminae of L5 may be postponed until the fifth or sixth year of life. A common developmental aberration is posterior wedging of the body of L5, which persists into adult life. It has no pathologic significance. The intervertebral disc between L5 and S1 may be narrower than the disc spaces above this level. This also has no pathologic significance unless there are some other radiographic criteria of disc disease, such as sclerosis of the opposing bony margins of the interspace, irregularities of the opposing margins, or changes in the adjoining ligaments. The plane of the zygapophyseal joints in the lumbar spine ordinarily make an angle of about 90 degrees with the plane of the sacroiliac joints. It is probable that slight alterations in the plane of the zygapophyseal joints, particularly the ones between L5 and S1, are related in some patients to instability and pain in the low back. Encroachment upon the intervertebral foramina in the lumbar region may cause back pain. Encroachments can be caused by the vertebral bodies themselves, the intervertebral discs, the articular processes, the articular capsule, or hypertrophic bony spurs. Meschan and Meschan consider functional radiographic studies of the lumbar spine to be important in assessing the cause of low-back pain. They make lateral films with the spine in the neutral position, hyperflexed, and hyperextended. They make anteroposterior films with the spine in the neutral position and bent to the right and to the left. Areas of relative rigidity in the lumbar spine may indicate the site of pathologic changes in the intervertebral discs or zygapophyseal joints. A method of studying alignment of the vertebrae in the low back is described, and its use in detection and estimation of the degree of

spondylolisthesis is discussed. The zygapophyseal joints are true synovial joints and are subject to all of the diseases which affect other synovial joints. They are best studied on the oblique views of the lumbar spine. In a lateral roentgenogram of the spine, a line drawn through the middle portions of the lower thoracic and upper lumbar vertebral bodies should fall directly over the superior margin of the sacrum. If it falls anterior or posterior to the sacral promontory, one can assume that a state of instability exists in the low back. In cases of scoliosis of the spine erect anteroposterior films are made in the neutral position and then with the patient tilted to the right and to the left. If the curvature remains constant during tilting, one is dealing with a primary curvature. If the curvature tends to correct itself, it is a secondary type.

WEILAND, Grove City, Pa.

AN ETIOLOGIC STUDY OF BACK PAIN. R. K. GHORMLEY, Radiology 70:649 (May) 1958.

Ghormley reports on 2,000 patients who were seen at the Mayo Clinic during one year and who complained of backache. These 2,000 represented only 40% of the patients seen there for this cause during that period. It is not stated what method of selection differentiated the 40% reported from the remaining 60% who were not included in the study. Twenty-nine different diagnoses are tabulated as the causes of backache in these 2,000 patients. It is not stated how the decision concerning the cause of backache was arrived at in any individual case. The commonest cause of backache was found to be osteoarthritis (degenerative joint disease), which was thought to account for the symptoms in 26% of the patients. In 22% of the patients a herniated intervertebral disc was suspected, but not necessarily verified. In 19% of patients a cause for the backache was not found. Backache brought on by activity and relieved by rest was found in 8% of the patients. These patients are listed as showing "static disturbances." About 6.5% of the patients were found to have rheumatoid spondylitis, although not all of these patients showed roentgen changes suggestive for or diagnostic of this disease. A history of pain and stiffness in the morning, obvious limitation of motion in the spinal column, and limitation of chest expansion are important diagnostic features of the early phases of this disease. Other diseases, each accounting for 1% to 3% of cases of low-back pain, included coccygodynia, previous trauma, spondylolisthesis (2.2%), tuberculous spondylitis, osteoporosis, recent trauma, and recent fractures.

WEILAND, Grove City, Pa.

News and Comment

ANNOUNCEMENT

The Archives of Neurology and Psychiatry was first published in 1919. At that time neurology and psychiatry were considered related subject fields and it was thought one journal would serve both adequately.

Over the years, psychiatry has been emerging as a distinct specialty. The volume of literature has increased to such an extent that official publications reporting psychiatry either could not absorb it or felt the need to condense the material to accommodate more contributions. Psychiatrists began to feel also that the Archives of Neurology and Psychiatry should allot more space to psychiatry, that its emphasis over the years had been neurological.

In July, 1956, an effort was made to give equal emphasis to both neurology and psychiatry by dividing the Archives of Neurology and Psychiatry into a two-section journal, with an editorial board for the Section on Neurology and a separate board for the Section on Psychiatry. This division had the effect of reducing the number of pages devoted to neurology, and the result was late publication dates for accepted articles, with the natural development of a large backlog. More psychiatric manuscripts were now submitted to the Archives, and only very high editorial standards and a high rate of rejection prevented a large backlog from forming.

The final development is to publish two separate journals. The division is prompted by the demand by both neurologists and psychiatrists for more text pages; by the neurologists, who feel the quality of a journal devoted exclusively to neurology can be much improved, and by the psychiatrists, who believe it is more realistic to recognize neurology and psychiatry as distinct clinical specialties. Consequently, July, 1959, will see the introduction of these two journals—the *A. M. A. Archives of Neurology* and the *A. M. A. Archives of General Psychiatry*.

A REQUEST FOR CERTAIN AUTOPSY MATERIAL TO FURTHER NORMATIVE RESEARCH ON THE MYELINATION OF THE HUMAN NERVOUS SYSTEM

The undersigned are currently engaged in a study of the standard criteria of the normal myelination of the human nervous system from birth to puberty. The purpose of the study is to establish comparative age gradients of normal myelination for comparison with the retarded and pathological myelination, employing routine histological techniques in common usage (Heidenhain, Weil, Loyez, and Klüver-Barrera methods) for staining myelin.

The autopsy material of reasonably normal cerebra and spinal cords of human infants and children is difficult to collect from any single geographic area of the population in a statistically sufficient number and age distribution from birth to puberty.

Through the medium of this journal we appeal to the departments of pathology and to medical institutions authorized to perform autopsies to make available to us such pertinent cerebra and spinal cords of infants and children up to puberty as they may be willing to entrust to us for study and may deem practicable.

The specimens of cerebra of infants and children should be reasonably free from disease processes which caused death of the infant or child. The cerebra should be removed whole with the brain stem and cerebellum and should preferably be perfused immediately after removal from the cranium with 200-300 cc. of the usual 4% to 10% formalin solution through the internal carotid and vertebral arteries. The so-perfused specimens should be suspended in at least ten times their volumes of formalin for a few days to two weeks. When reasonably fixed, they should be placed in a cellophane bag and packed with ordinary Vaseline in a tin can of suitable size. The tin cans and packing material will be supplied on request. The sealed tin can with the specimen and information on it should be sent by Railway Express, C. O. D., to:

Myelination Laboratory
Warren Anatomical Museum
Harvard Medical School
25 Shattuck St., Boston 15

Specimens so received by us will be prepared in gapless serial whole-brain celloidin sections. The investigators agree to supply the sender of each pertinent specimen with a complete set of unstained sections at intervals of every 20th section through the entire specimen. The specimens which should be found by us not suitable for purposes of this study will be returned to the sender at our cost.

All expenses entailed in preparing, packing, and shipping the specimens will be met by the Myelination Laboratory.

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SECTION ON
PSYCHIATRY

Report on Liaison Psychiatry at Michael Reese Hospital, 1950-1958

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I. History

This report is the product of the combined experiences of a group of psychiatrists (approximately eight at any given time) who worked with the attending and house staff of the general hospital at Michael Reese. This work was started in 1950, as a development of the regular consultation service. The primary goal was to bring about a more effective exchange of information between the psychiatrists and the physicians in the general hospital, and, secondarily, to teach the psychiatric resident the fundamentals of the psychosomatic approach to medicine.

This method was elaborated as a natural development to previous attempts in this direction. After World War II, a psychosomatic clinic was established and carried on by Dr. Roy R. Grinker for five years. A group of interested internists attended weekly two-hour meetings, where cases were assigned to them for treatment and were discussed by the attending psychiatrists. This program was interrupted when the internists became involved in serious transference reactions with which they were unable (and also untrained) to cope. Such an approach proved unrealistic.[1]

In order to circumvent this problem, a less ambitious and more realistic program was adopted. This resulted in the psychosomatic case conferences conducted by Dr. Herman M. Serota, to which interested specialists were invited. These conferences proved to be instructive to the psychiatric resident but did not offer the type of approach considered most valuable to the practitioner. It seemed necessary that there be a more sustained and closer personal contact between the psychiatrist and the specialist. Originally patterned after the liaison service at Mount Sinai Hospital of New York,[2-4] a third program was evolved which resulted in our present Liaison Psychiatry Service.

The services were structured as follows: Seven to ten psychiatrists on the attending staff of our Psychiatric Institute were assigned to the various services of the general hospital. These included (1) male medicine, (2) female medicine, (3) male and female surgery, (4) obstetrics and gynecology, (5) chest medicine, (6) surgical spe-

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Drs. Ernest Rappaport, Henry Seidenberg, and Alvin Suslick participated in the many discussions incident to organizing the data. Dr. Herman M. Serota, during his five years as Chief of Liaison Psychiatry, organized the new service and did much to define and elaborate many of the principles discussed here.

cialties, (7) ophthalmology, and, more recently, (8) physical medicine. The psychiatrist and psychiatric resident worked with the attending personnel on each service, via ward rounds, bedside teaching, interviewing of patients, etc. The experiences gained on the wards were exchanged among the psychiatric liaison personnel at semimonthly meetings. The essence of the experience gained over eight years is the subject matter of this report.

II. Introduction

The many areas in which liaison psychiatry has made effective contributions can best be discussed by dividing them as a matter of convenience into two major categories: (1) the consultation-type functions and (2) the specifically "liaison" functions. The former comprise the services usually rendered by a psychiatrist summoned as a consultant; the latter constitute relatively new functions of the psychiatrist as he works over an extended period of time on the various nonpsychiatric divisions of a general hospital.[1-9] The considerable experience and contributions in this latter phase of liaison functioning will be described after a detailed presentation of the more familiar consultative aspects.

III. Consultation Services Rendered by Liaison Psychiatrist

A. Problems Primarily Psychiatric.—On any given ward in a general hospital there are commonly problem cases in which the difficulty is primarily a psychiatric one. Among these are any of the psychotic reactions, such as a medical or surgical patient who suddenly loses contact with reality, becomes abusive or flagrantly uncooperative or is potentially suicidal. It is of interest that the incidence of this type of emergency has become minimal since the effective functioning of a liaison psychiatry service. This fact is due to the detection of such cases in nascent stages by the psychiatrist and by the evolution of an attitude on the part of nonpsychiatric personnel that either alerts them to earlier diagnoses or actually forestalls the development of unmanageable psychoses. For example, some services are much more tolerant of disturbed patients than in the past and are willing to explore the possibilities of ward management rather than make immediate transfer to a psychiatric service. The use of the newer drugs is sometimes helpful. For example, a patient who developed a severe anxiety state with disorientation and behavior disturbing to other patients after a cerebrovascular accident was quickly controlled with oral promazine (Sparine). Because the medical resident was familiar with psychiatric techniques as a result of his contact with liaison psychiatry, he was able to tolerate his feelings about the patient and to experiment with ward management. The fact that the liaison psychiatrist was available as a consultant in the situation facilitated the whole process.

On the chest service, because of the more intimate and prolonged relationship of doctors and their chronic patients, psychiatric complications are tolerated to a greater degree than on most other services. Even serious psychiatric disturbances can be managed on a chest service with the supervision or direct therapy by the liaison psychiatrist or resident. Specific problems range from a severe anxiety state reactive to the diagnosis of tuberculosis, to a severe paranoid outbreak reactive to the final awareness of the size of a surgical scar and the degree of surgical intervention. One woman felt she had been grossly mutilated and contemplated litigation against the hospital and staff. This was forestalled by supportive therapy on the part of the medical and nursing personnel under the guidance of the psychiatrist.

In the few situations of obviously unmanageable psychoses, the liaison psychiatrist or resident helps to transfer the patient as expeditiously as possible to an appropriate psychiatric facility.

The problem of suicide occurred only occasionally among service patients. After

a patient who has attempted suicide is medically recovered, the usual problems of psychiatric evaluation present themselves and can be managed on the basis of clinical judgment.

Among the ward cases are problems which are also primarily psychiatric but of a neurotic degree rather than psychotic. Some of these problems can be managed by supportive therapy by the liaison psychiatrist or resident while the patient is on the ward. For example, an acute hysterical conversion in an obstetrical patient was temporized via a narcosynthetic management. Anxiety reactions or uncooperativeness to acute organic illnesses can also be effectively managed by immediate therapy. Chronic neurotic reactions can be referred to the psychiatric outpatient clinic, for which the liaison service functions as a screening agent.

Occasionally psychiatric symptoms may be the first manifestations of organic brain disease. A psychiatrist can sometimes be the first to detect such a disorder and can make an effective clinical teaching contribution in the training of nonpsychiatric personnel in such cases. It is well to be prepared with material for a 10-minute discussion on the subtler psychiatric manifestations of organic brain disease and the diagnostic procedures available through psychiatry (psychiatric examination, EEG, Rorschach, social-service-obtained history, interview with relatives). A working knowledge of neurology can be invaluable.

In one case a diagnosis of Pick's disease was eventually established on the basis of the psychiatrist's bedside observation of inappropriate smiling, subtle euphoria, and perseveration. Social-service history requested by the psychiatrist revealed a two-year period of deterioration in typing skill. The Rorschach test was suggestive of an organic process. The pneumoencephalogram was confirmatory. This case probably would not have been referred for psychiatric evaluation if a liaison service had not been in operation.

B. Problems Primarily Medical.—The psychiatrist is also asked for his clinical judgment and advice concerning problems which are primarily not psychiatric, as in the management of medical or surgical cases. He often is asked for help on obscure diagnostic problems.

Management problems can often be solved with the information elicited during a brief psychiatric interview and by the psychotherapy incident to it. For example, a 45-year-old woman with a recent coronary occlusion was not cooperative in her bedrest regimen. She insisted not only on not staying in bed but also on helping other, nearby patients. She was alert and intelligent. Brief interview revealed a history of lifelong "doing" for others. She was a divorcee and had supported two children to adulthood. She worked too hard as a waitress. Out of a feeling of unworthiness, she masochistically earned her love from others. To be a bed patient, waited on by others, was an ego-alien concept. It took only 10 minutes to sketch out the personality picture. She was told in a firm but kind way that it was now her turn to be cared for, she had earned it, and her health depended on it. The interview was evidently sufficient for her to form a positive transference, which was maintained by brief friendly contacts when the liaison psychiatrist visited the ward. She became a model patient immediately after the interview and remained so.

A 22-year-old man was hospitalized for severe infectious jaundice. Ward personnel members were startled by the patient's insistent demand that he be discharged even "against advice." Brief interview revealed he was the sole support for his mother and four younger children. During visiting hours they urged him to return home, since they were desperately in need of the income he provided. The dilemma was soon resolved by referral to the social worker, who arranged for financial aid, and the patient became cooperative for the remainder of his treatment.

The liaison psychiatrist was asked to see an elderly woman with chronic gastric bleeding who refused surgery. A malignancy was suspected, but surgery was imperative to control the bleeding. Interview revealed she lived alone in the old-people's home, had no relatives, and could ask no one for counsel. Also, she was old and asked to be allowed to live out her remaining short time without surgery. Her point of view was sympathized with, but she was told she was in our hands and she must let us make the necessary decisions for her. She responded resignedly and was cooperative in surgery, which she survived with only the usual distress.

Other management problems are solved by medical personnel with the aid of the psychiatrist in the form of advice or information crucial to diagnosis or management. For example, an intern asked for help with a middle-aged woman who was a management problem in that she asked for constant changes of medication and had numerous ever-changing complaints. In a very brief interview it was determined she was a refugee with a most disheartening life history, but who at the moment used a hypochondriasis as a contact and control maneuver. The intern, who was trying to apply what he had learned from psychiatry, attempted to be kind and solicitous, a treatment which was exactly wrong for this patient. He was advised to be firm and matter-of-fact with her, prescribing only one medicine in a clinically authoritative manner, and to spend relatively little time with her. This was carried out, with relief to both intern and patient. The intern was confused by the fact that he had successfully managed an anxious patient with a kind, supportive attitude and thought it should work with this hypochondriacal patient, too.

Another category of management problems has to do with the disposition of patients to rest homes, other hospitals, etc. The psychiatrist often can facilitate liaison with social service and expedite some dispositions.

In addition to management problems, a liaison ward service also presents diagnostic problems. Sometimes an undiagnosed malignancy may first be suspected by a psychiatrist.[3,10] In other situations, a negative psychiatric diagnosis often helps to focus organic diagnosis and management. Occasionally a psychiatrist can specifically state that a given clinical problem is definitely organic, although not knowing its specific site or nature.[11] The psychiatric interview often catalyzes a more thorough history taking, which may reveal crucial information not otherwise obtained and essential to diagnosis or management. For example, a middle-aged woman being interviewed primarily as a teaching maneuver revealed she was a chronic alcoholic. Only after the interview did the medical resident advise the psychiatrist that a diagnosis of cirrhosis had been made, the etiology being until then unknown. She had been asked specifically several times about alcohol consumption and had denied abnormalities. Evidently the attitude of tolerance she felt in the interview allowed her to venture the disclosure.

Another ward problem consists in being asked to help with making a decision regarding surgery, using possible psychiatric postsurgical complication as a contraindication. Experience proved that the best policy was to insist that surgery be decided on medical criteria alone and that possible psychiatric complications be treated if and when they appeared. An interesting experience had to do with a 35-year-old woman with mitral stenosis and cardiac decompensation. It had been determined that mitral commissurotomy was indicated. However, she also was at times depressed and irrational. There was a history of previous psychiatric-hospital treatment. Psychiatric advice was that surgery be proceeded with and that any psychatric complication would have to be contended with when it developed. The day before surgery the ward nurse (highly competent and experienced) approached the psychiatrist with her misgivings about the emotional state of the

patient. The psychiatrist still felt that, since surgery was considered essential, no psychiatric criteria could take precedence. In retrospect, this unusual conduct of the nurse was remarkable, since the patient died during surgery. The nurse's misgivings were due to her clinical judgment, facilitated by her constant and intimate contact with the patient.

Where elective surgery is contemplated and a conclusion is difficult to reach, an assessment of the emotional state of the patient may be helpful in arriving at a decision.[12] A woman who had had one child with bilateral congenital cataract was pregnant for the second time. Her blood serum was found to be Rh-negative, with a rising titer. Toward the end of her pregnancy the problem of sterilization arose, and she was emphatic that it be done. A psychiatric interview revealed that she felt there was something very destructive in her which was being transmitted to her children. The liaison psychiatrist recommended that a decision be postponed until after the birth of the child. The child was born; exchange transfusion was performed, and in a few days the infant was completely normal. Recognizing that she could give birth to normal children, the patient was thankful that no tubal ligation had been performed.

There are a few cases in which candidates for surgery have their whole surgical course favorably influenced if the liaison psychiatrist or resident follows them psychotherapeutically from the presurgical through the immediate postsurgical phase.

During the course of the service, interesting problems have arisen which have led to research projects, some of which have been reported elsewhere.[11-14]

Another important ward problem has to do with helping to establish a clinical atmosphere by emphasizing clinical observation and approach rather than overemphasis on laboratory examinations. This will be discussed in detail below.

IV. Liaison Aspect of Liaison Psychiatry

In this section, the practical applications of psychiatric and psychoanalytic knowledge in bedside teaching in helping to develop an effective doctor-patient relationship are considered.

The premise on which this aspect of liaison psychiatry is based is that younger physicians do not understand the therapeutic significance of a clinical approach to a patient, or the importance of a patient's transferrence in the response of a patient to a therapeutic regimen.[16-30] Efforts in this type of teaching are most effective with interns and residents, whether via bedside teaching, casual ward discussions, or interviewing a patient.

A considerable effort can be effectively expended in using one's knowledge to teach respect for the patient. Owing to the undue emphasis on the "scientific" aspects of medicine, many young doctors do not learn that patients are people whose feelings must be respected. More experienced clinicians also may treat ward patients disrespectfully. When the liaison service was first instituted, case histories were discussed in front of the patients; patients were examined without benefit of screens; medical personnel smoked, read newspapers at the bedside, or carried on personal conversations irrelevant to the examination at hand. Similarly, radios, television, and housekeeping noises remained unchanged during ward rounds.[31]

All these parameters were changed slowly and tactfully by precept or by direct suggestion. Patients are no longer discussed at the bedside; screening during physical examination is carefully observed; the importance of a quiet, attentive atmosphere on the ward is more clearly recognized. The young physician is thus taught simple elements in a clinical approach to a patient, in contrast to an impersonal attitude fostered by an overemphasis of "scientific" and laboratory aspects. Liaison can help teach the art of medicine scientifically.

As a result of this type of teaching the physician achieves a perspective on his importance as a person to the patient, and the patients respond to such demonstrations of respect with increased cooperativeness and with many fewer episodes of behavioral complications.

Another potential function of the liaison psychiatrist which gradually became apparent is the necessity of helping doctors learn respect for themselves. Experienced physicians have learned this through error, intuition, and awareness of their own competence, but how to teach this to younger personnel?

One practical approach to this problem is to emphasize the importance of transference. In discussing transference with young physicians, it can be pointed out that there are two elements in a patient's transference reactions. One has to do with the realistic needs of a sick patient for dependence on a technically trained person. The patient expects expert help and selects a physician specifically for this. The second element in transference is an unrealistic one and has to do with the reawakening of infantile impulses for which gratifications are unconsciously expected from the physician. Such transferences will develop regardless of the physician's personality if a certain minimum of dependence is allowed.

Some young physicians do not realize that at last they are the ones to whom patients look for help. Dependence of patients on interns and residents is especially true on the service wards. The importance of a patient's dependence on him to the maturation of a physician-in-training was illustrated by the following example. An intern new to the hospital received a narcissistic bruise when a patient reacted apprehensively to his attempts at venipuncture, but confidently allowed the resident to proceed. The intern viewed this as evidence of his own inadequacy, whereas in reality he was technically competent. It was important to have explained to him that the patient was cooperative on the basis of experience of her dependence on the resident during the preceding month. As a result the intern achieved a perspective on the transference elements on the patient's part plus an understanding that what he does and how he does it as a person makes a difference to the patient. It was also pointed out to the intern that he should view this not as a reflection on him personally but as a behavior trait common to many patients. In addition, he was taught that in the future he would do well to maintain a scientific objective attitude toward such conduct, maintain his clinical approach, and, the next time he confronted the patient, conduct himself as though nothing untoward had happened. His function is to present himself consistently as an agent of help and support. Only a psychiatrist can bring scientific understanding in such a situation, and only a psychiatrist can bring a fund of scientific tact enabling him to teach these aspects of the doctor-patient relationship in a way helpful to the young physician.

Another maneuver one can use in teaching a physician is to convey one's own respect for him, for example, by consistent punctiliousness, by reliability, and by answering questions simply and directly in language he understands. It requires a considerable mental nimbleness to translate a medical question into psychiatric concepts, find the answer in psychoanalytic terms, then retranslate it quickly into language the physician can understand and still not be condescending.

Once a relationship based on mutual respect is established, the medical staff is able to bring up problems that otherwise would not have come to light. The psychiatrist's respect enhances the physician's self-respect. One element in the resistance of nonpsychiatric personnel to a liaison relationship is the fear of exposing lack of knowledge and fear of criticism. But once the testing-out phase is weathered, a mutually beneficial working relationship can be established.

The liaison psychiatrist also is in the unique position of being able to foster the

image of a bedside clinician. Much current medical education tends to overemphasize the laboratory aspects of medicine and fails to consider the influence of the physician as a person on his patients. A simple example is that some inexperienced doctors do a physical examination gruffly and impersonally. Tactfully pointing out that such examinations are being performed on a fellow human and that gentleness is in order serves to put the interpersonal relationship in perspective. By teaching such a clinical approach, the liaison psychiatrist can serve as an ego-ideal and foster the image of a bedside clinician.

During ward rounds there used to be an excess of discourteous joking and unnecessary interruptions. This was corrected over a long period by tactful suggestions on the psychiatrist's part. For example, it was common during a physical examination by the attending man for the resident or adjunct to ask the liaison psychiatrist questions concerning other patients. It can simply be indicated that the examination being conducted warrants full attention and that other matters could be discussed at a more opportune moment. By such uncomplicated devices tending to increase the atmosphere of dignity and simple good manners the doctor's awareness of his importance to the patient is enhanced.

Another aspect of the liaison psychiatrist's function is that he serves as an ambulatory superego.[32] It was a common experience to observe physicians go on their good behavior when the psychiatrist attended ward rounds. They often tried to impress the psychiatrist with their clinical knowledge and teaching abilities; also, they treated patients more kindly.

There are many instances of interpersonal conflict between various members of the house and attending staff. It was often possible to mediate or modulate interpersonal competitiveness. For example, when there are two residents on service simultaneously, rivalries are particularly acute. A considerable tact is required to maintain a teaching atmosphere and yet maintain a disciplined leadership. The problem of a bright intern is also of interest and requires judicious reining of his enthusiasm, and yet encouragement to express his ideas and observations. One rewarding experience was with an intern who had a language handicap and on rounds did not seem able to hold up his end of responsibilities. But one morning there was an opportunity to spend some leisurely time with him, and he proved to be a most intelligent intern and demonstrated an unusual knowledge of clinical, and even psychiatric, literature. The fact that a psychiatrist is available to perform this type of service cannot help enhancing an intern's attitude toward his training and stimulate a loyalty to his hospital. This could be of significance in the current recruitment problems concerning interns.

The clinical interview can be used as the one most effective maneuver in teaching what psychiatry has to offer to medical personnel. A casual interview of from 5 to 15 minutes usually is adequate. The primary aim of the interview is to sketch out briefly the personality type and background of a given patient, so that an interpersonal relationship between doctor and patient can be more scientifically fostered.

One can begin by having the patient review the medical history, then ask for family history, work history, marital situation, and current living circumstances. Often crucial medical information is obtained which is of importance to medical diagnosis.

Even such a superficial psychiatric history suffices to distinguish a given patient from all other patients and teaches the hospital staff that some of their patients are interesting people and merit personal attention and interest. For example, the cultural and social stratum from which a patient comes helps the responsible physician to gauge what to expect from the patient in the nature of cooperativeness. He can determine more scientifically what sort of an approach to use, such as, for example, the contrast in approach to a

schoolteacher versus that to a numbers-racket flunky, or the contrast in approach to a woman contentedly married with attentive children versus that to a masochistic immigrant married to an abusive alcoholic husband. Only psychiatry seems able to teach this type of scientific personal approach to a patient.

Aside from the factual knowledge which evolves from such an interview, the residents and interns learn a professional approach to a patient simply from listening to the psychiatrist's tone of voice as he talks to a service patient, his kindness, the tolerance, the attitude of not sitting in judgment. Similarly, they learn from witnessing how a patient responds to such an approach.

It is well to terminate an interview after having demonstrated a simple clinical vignette—e. g., the demonstration of a patient's anxiety; the elicitation of significant material about current conflicts which explains difficulties in ward management; the effect of the illness on the patient and the effect of the patient's emotional state on the illness; the importance of follow-up on a surgical patient; when and how to be firm; limitations of psychotherapy; the necessity of admitting psychotherapeutic untreatability by a nonpsychiatric physician.

Simple elements in the countertransference can be brought out; for example, therapeutic ambition as exemplified by a physician's negative response, and even anger with a patient who does not respond to his reassurance or other palliative maneuvers.[33] Another simple subject to demonstrate is how the patients fulfill the doctor's narcissistic needs. Sexual countertransference reactions also come up and can be discussed in a casual setting. Similarly, the subtler evidences of a patient's transference can be demonstrated.

After the patient has been dismissed from an interview, an informal discussion can be held on such subjects as why a physician evokes a transference, the importance of extra time spent with a patient, the dividends resulting from personal interest, even the increased effectiveness of medications in the setting of a positive transference.

Other matters, such as the handling of relatives, obtaining surgical permits, etc., come up. A frequent topic is what to tell a patient with a malignancy. Using clinical experiences as the basis for a series of round-table discussions, we have examined this problem in detail. With the number of variables to be considered, no absolute generalizations can be made.[34-36] Malignancies vary in their method of spread, rate of growth, susceptibility to irradiation, etc. Prognosis may be good, doubtful, or hopeless. Each patient's present life situation and past experiences differ considerably. Trying to limit the number of variables, and considering only cases of incurable malignancies, we still found that we could not come to any definitive conclusions. This, of course, indicates the complexity of the problem. Some of us felt that we should be guided by the manner in which the patient had most effectively handled his anxiety in the past. Those patients who faced the reality aspects of past problems should be told, while those who used denial in any form should have this denial supported. Others felt that the threat of death is almost always reacted to with various means of denial, so that in all cases the physician will find himself supporting this denial. The support of a psychiatrist to such an approach, with exchanges of clinical anecdotes during ward rounds, has been worth while.[34-36]

In summary, the "liaison" aspect of liaison psychiatry has to do with the scientific teaching of the many facets of the doctor-patient relationship, using such maneuvers as bedside teaching and brief clinical interviews of individual patients.

V. Relationship to Social Service

Since the social worker is by training alert to the intrafamilial and interpersonal aspects of illness, and has special knowledge in the economic and administrative aspects

of medicine, she is often essential in arranging the after-care of hospitalized patients, as well as being in a position to furnish important information for the medical history when it is indicated. Social-service history is also often of significance in aiding a medical and/or psychiatric evaluation of a patient. There are times when a social worker can be helpful in the supportive management of a patient's family, as in the following case.

Mr. A., a 28-year-old white married Catholic, was hospitalized awaiting surgery for an aortic stenosis. In the weeks of preparation, including cardiac catheterization, Mr. A. grew progressively more restless, and his physicians were apprehensive about his attitude toward surgery. Psychiatric consultation was requested. It was learned from the patient that he feared cardiac surgery, for it might incapacitate him to the point where his dissatisfied wife might really go through with her threat to leave him; he felt that she had grown disgusted with his physical weakness and wanted some one stronger who would be able to provide for her entertainment. He already had delusions of his wife's unfaithfulness. It was not surprising to hear that he fantasied surgery would turn him from a man into a woman.

The social worker was able to bring the following material to bear on the case. The wife, a 26-year-old woman, was good-looking and seductively overdressed. Her frustrations in caring for two young children, working to supplement the family income, and being supportive to a husband she did not believe was really ill were many, and there was no doubt she was fantasying an extramarital affair. But she was also rather fearful of her fantasies.

Since Mr. A. refused psychiatric care, the resident medical physician was supervised in the superficial psychotherapy, allowing him to be permissive enough to let the patient go home on passes between diagnostic procedures and prove his masculinity. The social worker saw Mrs. A. in a supportive relationship emphasizing (*1*) the reality of Mr. A.'s illness; (*2*) providing her with an emotionally supportive relationship, as well as one in which realistic economic planning could take place; (*3*) instructing her on where to obtain scientific contraceptive information.

When the considerable tension between Mr. and Mrs. A. had been reduced, Mr. A. underwent surgery, with little of the emotional upheaval that could easily have occurred.

Summarizing, therefore, the liaison position of the social service worker, it can be seen that her multiple roles can be readily utilized to bring a more comprehensive treatment program into being.

VI. Relationship to the Psychiatric Resident

The psychiatric resident serves as a full-time stand-by for the psychiatrist, often effecting emergency service of a therapeutic and administrative nature. Optimally the resident screens each patient on his service with a brief interview, calling attention of the psychiatrist to problems of interest. He also serves as a liaison contact between the house staff and the psychiatrist via his professional and social contacts. A common pedagogical problem is to train the psychiatric resident to translate his technical knowledge into language understandable to the nonpsychiatric personnel. This can most readily be effected by precept and direct tactful discussion. It is of value to the resident to witness a discussion of a patient which can be of help to his management without recourse to jargon and esoteric dynamics. A further training stratagem is judiciously to steer questions from the house personnel to the resident for experience in concise responses.

Also of value has been the practice of holding one of our semimonthly meetings as a dinner-meeting at which the liaison-psychiatry residents are guests and at which each resident presents cases of interest for discussion. Emphasis is placed on the function of the resident, as exemplified in the following case.

The patient, a 36-year-old Negro woman, was admitted to the hospital because of the complaints of chest pain, nausea, anorexia, weakness, and shortness of breath. She continued to suffer these symptoms intermittently during her first two weeks in the hospital. She had been admitted as an emergency case, and each attack of symptoms was treated in this way for the first few times. The physical work-up failed to reveal any basis for the severe symptoms. There was an indication that the rheumatic fever she had suffered in early adolescence had caused some cardiac changes, but this was not severe. The resident on the case suggested to the patient that they could not explain the severe attacks interspaced with periods of comfort. She responded violently, indicating

that she felt accused, and said that if there was nothing wrong with her she should see a psychiatrist. The resident agreed, and a consultation was arranged. When interviewed, the patient was initially very belligerent and defensive. She felt that she had been told there was nothing wrong with her; to her this meant some doctors were untrustworthy. She had been hospitalized at another hospital two years before, with similar symptoms, and she had remained there as a private patient for a month, at great expense to the family. She spent many days in an oxygen tent, and many tests were made. She improved but was told on discharge to take it easy. Since that time she had curtailed her activities, and the family became very protective. Her husband arranged to make only short runs on the railroad, and her mother spent many hours helping her with the house. She denied she had actually wanted to see a psychiatrist and felt he had been forced upon her. She went on to say that she had become ill while helping the family of a dead friend with the preparation of food following the funeral. The deceased friend had had heart disease also, and she had been told by the clinic doctors that she was not severely ill and could live for many years. The friend's death frightened the patient, and she began to fear the doctors were not telling her the truth about her condition when they reassured her. The psychiatric resident suggested that the doctors had done what they thought best for the patient, that they were not trying to deceive her, nor did they believe she was trying to deceive them. A number of friends and relatives, including her father, died during the year before her attack two years before. The psychiatric resident then discussed the case with the resident on medicine. They agreed that she had definite signs of an emotional disorder. At this point the medical resident talked at some length and heatedly of how he felt he had been taken in by her. It was suggested that she had not done this deliberately but, rather, that this was her way of appealing for support from an omnipotent figure. He reacted with some awareness that his anger was related to a feeling of frustration centering around how little he had felt he could do for her. It was suggested that he could do a lot by pointing out the realities of her situation as of the present and indicating as fully as he could the extent of the heart pathology and discussing in detail what she could or could not do. He agreed with this and indicated that he felt relieved to know that the psychiatric resident agreed she should be discharged soon. He talked with her that afternoon, and after a long talk she cried for a few hours, after which she said that she felt she could leave the hospital.

Two days later the patient left in good spirits and looked forward to her appointment with the resident at the medical clinic.

At the monthly meeting, the following questions became the center of interest: 1. What was communicated to the medical resident which allowed him to be more effective with the case? 2. Where did the psychiatric resident err? 3. Was there anything else he could have communicated?

The discussion brought out the fact that in the very area where the medical resident felt weakest lay his greatest strength. His feeling that he had been taken in by the patient could be replaced by a feeling of being needed when he was able to recognize, with the help of the psychiatric resident, that this was the manner in which the patient appealed for support. In addition, his feeling of uselessness was dispelled when he was able to see how the patient could be helped, and how quickly she responded to it.

The psychiatric resident erred in his use of the term omnipotence. He could not know whether the patient was looking for an omnipotent figure, and the use of this terminology could be of no help to the medical resident. The use of the word "supporting," or "parental," or "authority" figure would have been much more meaningful to the medical resident.

The psychiatric resident could have done more by illuminating the significance of the precipitating situation of the death of the friend by heart failure. This type of vignette has proved most effective in teaching the comprehensive approach to medicine.

It should be noted that the psychiatric resident did not attempt any reconstruction of the psychodynamics of the case. In fact, it was through this case that both residents were able to initiate an effective, mutually beneficial working relationship, which was maintained during their period of service on the same ward.

In the future this program will be supplemented with weekly meetings of the psychiatric resident under the supervision of

a part-time attending man and the formal establishment of a liaison program as part of the training curriculum for the house staff of the general hospital.

To sum up, the psychiatric resident makes definite contributions to the service ward. His constant presence in the hospital, his interaction with his medical and surgical peers on a social, as well as professional, level make it possible for him to act as a diagnostician, therapist, and teacher to the service wards, its personnel and patients. By doing so, he finds himself better prepared to take a respected place among practicing physicians, able to assume his responsibilities with greater ease, and to respect the responsibilities of other medical specialists.

VII. Relationship to Nursing Personnel

Establishing a working relationship to the ward's charge-nurse can be a worthwhile effort. Whereas residents and interns change service frequently, usually the nurse remains on the same service. On some services the same nurse has been in charge for several years, and can be an invaluable source of contact for problem patients. Because she has her patients under observation more intensely than any other professional person, she can often help with clinical evaluation and prognostication. At times she may ask for help in management or understanding of some patients' emotional states. Occasionally she may ask for help concerning a student nurse. On one service the liaison psychiatrist was instrumental in the referral of a student nurse for help because of the ward's charge-nurse asking about a possible disciplinary problem.

It must also be kept in mind that a charge-nurse can form a positive transference to the psychiatrist if both have been on the same service for a time. This can be a real asset to a working relationship. On one service it was necessary for the psychiatrist to chastise the nurse for her volatile attitude toward some patients and visitors. This allowed her to ventilate superficially some of her own tensions and furthered the mutual respect of doctor and nurse.

VIII. Liaison Psychiatry as a Phasic Process

Through the years of experience with liaison psychiatry, a pattern has emerged which has been more or less typical for all of the various specialties. The liaison psychiatrist is first received with a great deal of suspicion and some anxiety. Though he has been asked to come on the service, this usually is a token invitation. Experienced practitioners who have been recognized as outstanding men in their fields could hardly be expected to welcome men from another specialty who are there ostensibly to tell them something about their patients which will help in treating the patient more effectively.

The initial response of suspicion and anxiety will usually be handled by rejection of the liaison psychiatrist. This is never overtly expressed. On the contrary, the usual overt expression is that of welcome and thanks that the psychiatrist has made himself available. However, the covert rejection is accomplished in many ways, four of which can be described. First, the practitioners may find it difficult to make schedules coincide, or, having done so, they may later discover that something more important has arisen. Secondly, the practitioner may systematically avoid any reference to possible emotional problems in the cases up for discussion, or may ignore completely the presence of the liaison psychiatrist. Thirdly, they may recommend that the liaison psychiatrist see patients who are actually social service problems and have been considered by the service as unfruitful cases. Finally, they may try to rush headlong into poorly thought-out research problems which they hope might interest the psychiatrist, and which have the function of diverting the psychiatrist from his ward activity.

After some period of time, the liaison psychiatrist is usually able to make some real contribution. At the point at which something really significant has occurred, the psychiatrist may find a complete reversal of attitude on the part of the attending man (or men) on the service. He suddenly may be flooded by enthusiastic requests, and find that he is expected to have the answers to all of the problems. This includes not only the problems of the patients on the service but those of the attending man himself, or his family. These should be studiously avoided. This is a type of resistance that may be flattering to the liaison psychiatrist, but is no less a resistance. It is frequently more effective than the original rejection, since one is most easily trapped with the bait of one's own narcissism. After this phase has been worked through, the liaison psychiatrist is then able to establish the kind of a situation which leads to the most mutually beneficial relationship and most effective liaison psychiatry.

What must the liaison psychiatrist bring to the service which will allow him to obtain this effective relationship? This is one of the most difficult problems to solve. In some ways, it contains the very problems involved in how a psychiatrist makes an effective relationship with a patient. It also contains the problems involved in how a teacher makes an effective relationship with a student. And yet it contains more, since the psychiatrist is also there to learn. We have tried to define some principles, keeping in mind that this is really an oversimplification.

First, and obviously, it takes the ultimate in patience on the part of the liaison psychiatrist. Not only must he wait through long periods of "dry spells" but he must also recognize the various forms of rejections and resistances and still react to them in a constructive way.

Secondly, we, as liaison psychiatrists, must avoid the use of psychiatric terminology, which in many cases is little less than jargon. We sometimes try to impress by using technical language. This may be nothing more than empty generalizations used to hide our ignorance and to prove our value to the practitioner. He may be easily confused and may react with further rejection of the psychiatrist. This may be manifested by a repetitive use of the terminology, which makes it completely meaningless. And why shouldn't he? His technical language is perfectly clear to us. Why should he be burdened with a new language which is unclear to him, and may in some cases be used by us for personal reasons?

Thirdly, we must face the discouragement of not being able to exhibit our cherished dynamically involved reconstructions. Much of the gratification which accrues to a psychiatrist is his ability to see and describe the dynamics in a given case. This is fostered by the residency training, and is part of the goal of the case conferences. It seems to follow as a natural consequence of any history taking. In our work as liaison psychiatrists we must be satisfied with an adequate appraisal of the dynamics of the present situation. We cannot, in the time available, expect a thorough and deep understanding of the patient. Rather, we are interested in obtaining a vignette which allows us to demonstrate a point or points which can be understood and used by the practitioner. We have found this the most effective way of establishing and maintaining a relationship which leads to functional liaison.

Finally, it has been noted that many, if not most, of the problems involved in establishing an effective liaison can be overcome if the psychiatrist develops a respect for, and to some degree an understanding of, the work of the practitioner. Anything which includes an attitude of depreciation for the practitioner's specialty or the way in which he practices it inevitably proves disastrous to the liaison relationship. This is why we at this hospital try to select psychiatrists (for a given liaison service) who have had some interest in, and experience with, the specialty. We find that a real interest in the specialty, as well as a

developing respect for the way the specialist practices it, is most conducive to the development by the practitioner of respect for the psychiatrist. This inevitably brings about a constructive interchange of ideas, which is the foundation of a smooth-functioning liaison psychiatry.

In the process of creating this atmosphere of mutual respect, we have encountered one of our most challenging problems. Because of the fact that liaison psychiatry is relatively new, and most liaison psychiatrists have recently entered the practice of their profession, there is usually a marked discrepancy in years and prestige between the psychiatrist and the practitioner. It is hard for the practitioner to accept as a peer someone apparently so young and inexperienced, and even more difficult to accept him as a preceptor. As time and experience teach us more, this should be less of a problem. In the meantime, we have tried to minimize this problem by having the younger men work with the intern and resident on the service and the older and more experienced psychiatrist work more closely with the attending men. At the present time, we have found this procedure most functional. As we learn, and as we apply our knowledge with more effectiveness, this problem should resolve itself.

In summary, we have presented experiences in this relatively new field of psychiatric interest with the thought in mind of comparing experiences with those already in the field and as a reference for those who contemplate entering it.

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Behavioral and EEG Changes Induced by Injection of Schizophrenic Urine Extract

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Introduction

The present growth of interest in biological studies in psychiatry has been accelerated by a rapidly increasing body of knowledge concerning (1) the psychotherapeutic action of reserpine and chlorpromazine, and (2) psychotomimetic action of so-called hallucinogenic agents, such as lysergic acid and mescaline.

The recognition of a common denominator among these agents—an activated aromatic ring[29]—and the presence of a number of independent reports in the literature concerning the abnormally high concentration of various aromatic derivatives in the schizophrenic body fluids[24,25] led McGeer et al. to suspect the possible significance of aromatic metabolism in schizophrenia.

On the basis of the one-dimensional chromatographic analysis of several hundred schizophrenic and nonschizophrenic subjects, they found that the patients with acute schizophrenia generally excreted more aromatic compounds than did the nonschizophrenics. Further analysis with extracts of urine pools from groups of schizophrenic as against nonschizophrenic subjects indicated that there are several diazo-positive areas in two-dimensional chromatograms of schizophrenic urine extracts which did not appear in two-dimensional chromatograms of nonschizophrenic urine extract prepared under closely comparable conditions. These findings led them to the view that the difference in aromatic excretion between schizophrenics and nonschizophrenics may be not only quantitative but qualitative as well.[25]

Recently, Heath et al.[13] claimed that the administration of a protein substance extracted from the blood serum of schizophrenics produced the characteristics of schizophrenia in monkeys and human volunteers. Also, there are a number of reports in the literature on the peculiar physiological effects of schizophrenic body fluids. They include (*a*) production of a catatonia-like state in animals,[23] (*b*) production of hyperglycemia in animals,[28] (*c*) decreased stimulating effect on glucose utilization by tissues,[38] and (*d*) toxicity to mice[10,37] and to cell culture,[6] tadpoles,[8] etc. Although the results obtained, in general, have been variable and there has been much question as to the reality of the effects reported,[34] the possibility that the biological process of schizophrenia may involve some metabolic error, which, in turn, may produce excess amounts of some toxic substance or substances, cannot be excluded.

The present study was undertaken in order to test this possibility by evaluating the physiological properties of urine extracts with established chromatographic differences (*a*) from schizophrenics, and (*b*) from normal subjects. As a first step, the over-all effects of these urine extracts in the behavior and spontaneous electrical activity of the brain have been studied in animals and are described in this report.

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Materials and Methods

Two urine extracts* were used in the present study. They were made from pooled overnight urine samples of (*a*) a group of 20 schizophrenics at the Provincial Mental Hospital, and of (*b*) 10 of our departmental staff as controls. The schizophrenics were all recently hospitalized patients in the acute phase. They included both male and female representatives of the various forms of schizophrenia. Cases who received the tranquilizing drugs were excluded.

The aromatic materials were absorbed from the urine onto charcoal, the charcoal washed with water and then eluted with phenol-saturated water. The phenol was evaporated at low temperature and pressure. The residue was taken up in water, neutralized to pH 7, adjusted to a free-phenol concentration (Folin-Denis method) of 4 mg/ml. and filtered and sterilized before use. Each millimeter of extract corresponds to 5-10 ml. of urine. These extracts were kept in the refrigerator.

In the study, 9 cats and 12 rhesus monkeys were used for 19 and 21 observations, respectively. Prior to the injection of urine extracts, the behavioral pattern in response to the surroundings and to the experimenter was closely observed in each animal. The extracts were injected under the ether anesthesia. In three cats and one monkey electroencephalograms were recorded through the implanted cortical electrodes. In some animals the EEG was also taken through the scalp needle electrodes. Observations were carried out 6 to 12 hours following the injection, with the subject either in his cage or free in an examining room in which he could run about unimpeded. Cinematographic recording was done frequently. Although the intravenous injection produced an apparent pain along the injected vessel, a single intravenous or intraperitoneal injection of 1-5 cc. of these extracts did not produce any remarkable changes in the behavior or the electroencephalogram of the animal. Repeated intraperitoneal injection (1 cc. for 10 successive days) did not change their behavior, or the electroencephalogram either. Because the amount of extract available was limited, and because of the possibility of detoxification in the systemic circulation and of failure of passage through the blood-brain barrier at these concentrations, small amounts of extracts (0.1-0.5 cc.) were injected into the cisterna magna or lateral ventricle. Extracts were mixed and diluted at least three to five times with the aspirated cerebrospinal fluid immediately before the injection so as to minimize the possible influence of hypertonicity. Only results obtained by these latter methods are reported in this paper. Isotonic saline injected under the same conditions did not produce any significant changes in behavior or the electroencephalogram. About half of the animals were subjected to more than one injection in order to compare the effects of the two extracts or to check the reproducibility of the changes in the same animal. A repeated injection was done at least a week after the previous injection.

* Prepared by Drs. P. L. and E. G. McGeer. The detail of the preparative procedure and of the bidimensional chromatographic patterns of these extracts have been published.[24,25]

Results

Behavioral Changes in Cats.—Nine cats were used for 19 observations (9 for normal extract, 10 for schizophrenic extract).

Before the injection all cats used here were friendly. An amount of 0.2-0.5 cc. of an extract was injected into the cisterna magna under ether anesthesia. Following the injection most of the animals in both groups showed an ataxic gait, which was more pronounced in the hindlimbs. This ataxia was slight or absent within one hour following injection.

In the cases of normal extract injections, cats became less playful and usually crouched in a corner. A significant reduction in spontaneous activity was apparent, but, whenever caressed, the cats promptly responded by purring, or even playing with the experimenter. Otherwise, no specific behavioral changes were noted, except for a generalized seizure in one instance. On the other hand, none of the animals responded to caressing after the injection of schizophrenic extracts. Most of them appeared frightened. Stool and urine incontinence was noted in three instances. In two instances (Cats 17 and 19) the animals scratched the face and head intermittently with both forepaws for about 20 minutes.

In five instances the animal developed a peculiar state, which can best be called a rage state. A representative case is described in the following excerpt.

CAT 16 (Nov. 23, 1956)

1:35 p. m.: Injection of 0.25 cc. of schizophrenic extract into cisterna magna with 1 cc. of CSF under ether anesthesia.

5 min.: Moaning.

7 min.: Trying to stand up, ataxic.

10 min.: Frightened, does not want to be touched.

15 min.: Started mewing, trying to escape and to hide in dark corner.

23 min.: Aggressive, trying to bite; pupils widely dilated.

30 min.: Ferocious behavior, vicious biting.

40 min.: Hissing, growling continuously, viciously biting and scratching at anything near him.

50 min.: Same as above. Whenever something was shown to him, he would scratch and bite ferociously; pupils still dilated.

60 min.: Less vicious and still growling, hissing.

70 min.: No more growling, hissing; will bite when approached but less vicious.

85 min.: Does not bite, accepts petting—a completely different cat.

120 min.: Quiet, retiring, not angry even when handled roughly or when his tail is pinched.

Similar rage states were observed in four other instances (Cats 16, 17, 18, 19) for 20 to 60 minutes following the injection of schizophrenic extracts. Some of these animals (Cats 16, 17, 18) have also received a comparable dose of normal extract, on different days, but developed no rage state.

Four other cats (Nos. 8, 9, 15, 38) developed a peculiar behavior, which is different from the rage state described above. Both Cat 8 and Cat 9 developed automatism-like behavior. They became restless about 30 to 40 minutes after injection. The pupils dilated widely. They suddenly stood up and looked up, down, and back, as though they were searching for something. At this stage any moving object, or the presence of humans, did not attract their attention. Only when loud noises were made did they momentarily look for the source. When they were touched, they looked frightened and tried very hard to escape. This peculiar behavior gradually subsided about 40 to 60 minutes later. Electroencephalograms were taken on these two cats through implanted cortical electrodes. About 15 to 20 minutes after the injection of schizophrenic extract the EEG showed high-voltage 3-4 cps random sharp slow waves and occasional spike discharges. About 30 minutes after the injections, before the animals developed the peculiar behavior mentioned above, these high-voltage sharp slow waves and spike discharges

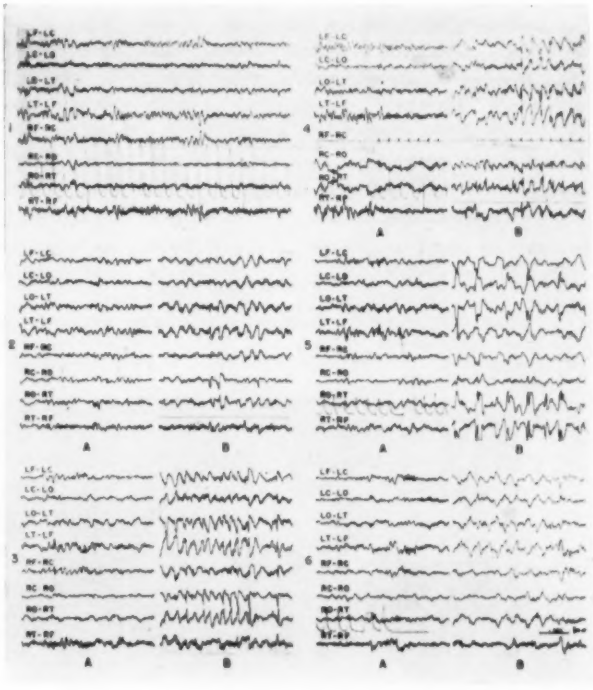


Fig. 1.—Electrocorticograms of cat following the intracisternal injection of 0.3 cc. of normal and schizophrenic urine extracts. The same cat, with implanted electrode, was used twice. Records following the normal extract are represented by *A* and those following the schizophrenic extract by *B*. *A* was taken about two weeks after *B*. (*1*) Normal control. (*2*) Thirty (30) minutes after injection of normal (*A*) and schizophrenic (*B*) extract. (*3*) One-hour after injection. Animal is showing automatism-like behavior (*B*). (*4*) Two (2) hours. Automatism-like behavior subsided (*B*). Photic stimulation (Channel 5 is connected to photo cell) produced a generalized high-voltage sharp slow wave (*B*). (*5*) Two (2) to five (5) hours. Animal resting (both *A* and *B*) but less responsive to caressing (*B*). (*6*) Five (5) hours. Animal appears to be normal (both *A* and *B*); however, sharp slow waves are still present in *B*.

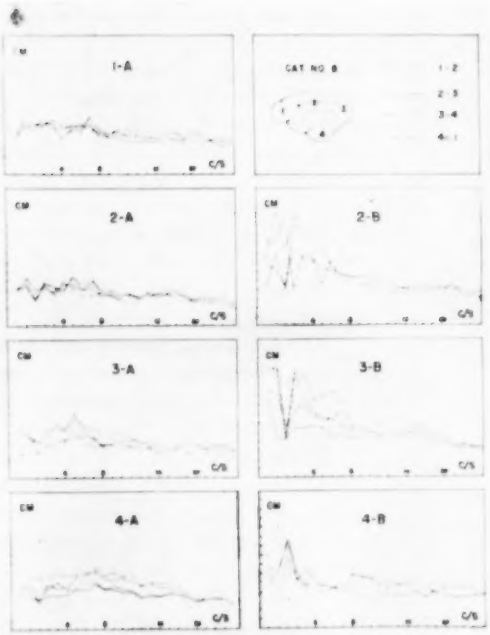


Fig. 2.—Electroencephalographic frequency analysis. An Offner frequency analyzer was used, measurements being made from bipolar recordings. The graph was made by measurement, in centimeters, of the height of pen deviation. The numbers on the horizontal line indicate frequency. Graphs on the left (*2A, 3A, 4A*) were taken after the intracisternal injection of 0.3 cc. of normal extract. Graphs on the right (*2B, 3B, 4B*) follow the intracisternal injection of 0.3 cc. of schizophrenic extract. Both observations were made in the same animal but on different days (about two weeks apart). (*1*) Normal control; resting; (*2*) 30 minutes; (*3*) 4 hours; (*4*) 24 hours.

became almost continuous. Although the animals' peculiar behavior lasted only about one hour, the EEG abnormality lasted more than five hours. Representative records are illustrated (Fig. 1).

The same animals (Cats 8 and 9) received the same amount of normal extract about two weeks later but showed no such behavioral or EEG changes. The frequency analysis of the EEG in both cases revealed that the schizophrenic extract induces a striking shift of frequency toward a slower band. A representative case is illustrated in Figure 2.

Another cat (No. 15) started to run around inside the cage, with a lot of foam around the mouth, about seven hours following the injection of 0.5 cc. of schizophrenic extract. He would stop suddenly and look into space, and hump his back—the usual posture which a cat shows when seeing an enemy. Sometimes he would go

Fig. 3.—Stuporous episode about two hours following the intracisternal injection of 0.2 cc. of schizophrenic extract. (*A*) This cat kept standing facing the leg of chair for about four minutes. (*B*) In another episode, the cat remained in this awkward position for about two minutes.

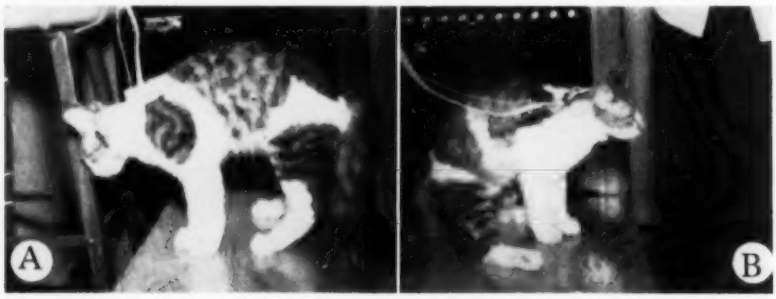


Fig. 4.—No response to pinching of right forepaw during stuporous episode. Note the calm expression.

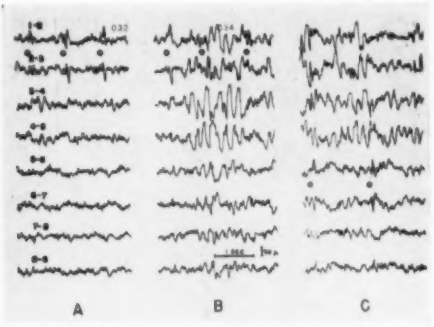


Fig. 5.—Evoked potentials during stuporous episode. Positions of electrodes are indicated in the brain chart of Figure 6. (*A*) and (*B*) Tapping (*a*) of left thigh; (*C*) click stimulation.

backward, watching a certain spot as if he were scared. When a white cloth was placed inside the cage, he appeared frightened. When he was placed on the white cloth, he growled and jumped off it.

The remaining animal (Cat 38) received a 10-month-old schizophrenic extract and showed a little different feature in behavior and EEG (all cats except Cat 38 received the schizophrenic extract during the first four months after this extract was made and refrigerated). About one hour after injection of 0.2 cc. of schizophrenic extract this cat showed remarkably diminished motor activity. He could be pushed forward en bloc. He walked very slowly, and, occasionally, he stopped suddenly at an awkward position and remained stuporous for a certain period (Fig. 3). During this state he frequently did not respond to the arousal stimuli at all (Fig. 4). Tapping of the part of his body, however, produced a series of evoked potentials at the sensory motor area, without arousing the animal (Fig. 5). Dur-

Figure 6

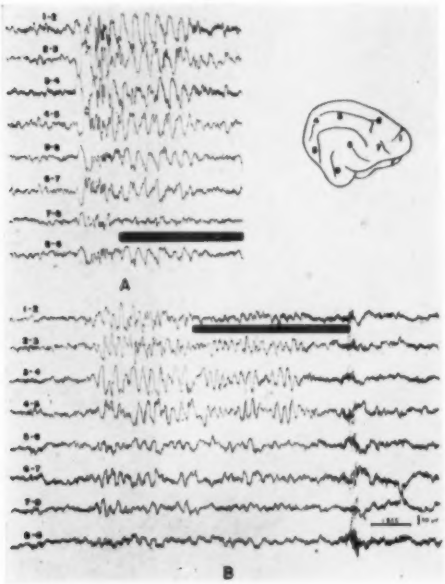


Fig. 6.—High-voltage burst activity during stuporous episodes. Black bar indicates pinching of left forepaw. (*A*) No behavioral response. (*B*) Animal became alert at the end of pinching.

Fig. 7.—Low-voltage fast waves during stuporous episode. Electrode arrangements are same as in Figure 6. No behavioral response to pinching of nose (black bar). Note slight increase of faster activity during the stimulation.

Figure 7

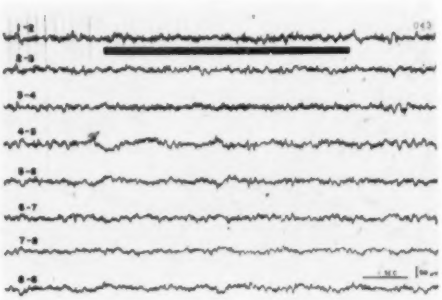


TABLE 1.—*Behavioral Changes Following Injection of Normal and Schizophrenic Urine Extracts into Cisterna Magna of Cat*

	Normal Urine Extract (9 Observations in 7 Cats)					Schizophrenic Urine Extract (10 Observations in 8 Cats)						
Cat No.	Dose, Cc.	Ataxia	Generalized Seizures	Affectionate Response	Others	Dose, Cc.	Ataxia	Generalized Seizure	Affectionate Response	Rage State *	Automatism-like State	Others
	Normal Urine Extract					Schizophrenic Urine Extract						
8	0.3	+		+	EEG	0.3	+		−		+	EEG
9	0.3			+	EEG	0.3	−		−		+	EEG
15						0.25	−		±			Stool & urine incontinent
						0.5	−		−		+	
16	0.25	−		+		0.25	−		−	++		
						0.5	+		−	+++		Stool & urine incontinent
17	0.25	−		+		0.5	+		−	++		Urine incontinence; scratching head by both forepaws before rage state
	0.5	+	+	+	Seizure about 10 min. after injection							
18	0.25	+		+		0.5	+	+ Status epilepticus		+		Tonic-clonic generalized seizure during rage state, becoming status epilepticus; stopped by amobarbital
19						0.2	+		−	+++		Scratching head by both forepaws before rage state
20	0.5	−		+								
	0.5	+		+								
38 †	0.5	+		+	EEG	0.2	+		−			Recurrent stuporus episodes; EEG

* Rage state: + = hiss, growl, and attempt to escape when approached; ++, hiss, growl, and bite, cat scratches when approached; +++, cat continuously bites, scratches anything near him, without provocation.

† This cat received the same extracts but one about 10 mo. old; all other cats received extracts of less than 4 mo. old.

TABLE 2.—*Behavioral Changes Following Injection of Normal and Schizophrenic Urine Extract into Lateral Ventricle or Cisterna Magna of Rhesus Monkey*

		Normal Urine Extract (11 Observations in 9 Monkeys)					Schizophrenic Urine Extract (10 Observations in 8 Monkeys)				
Monkey No.	Route of Injtn *	Dose, Cc.	Generalized Seizure	Docility †	Peculiar Behavior	Others	Dose, Cc.	Generalized Seizure	Docility †	Peculiar Behavior	Others
W-1	CM	0.4		+			0.4	+	+++	+	Vertical nystagmus for about 30 min.; seizure about 60 min. after injection
W-2	CM						0.5		++		
W-3	CM						0.5		++		
W-5	LV	0.5		++		Scalp EEG	0.5		+++	+	Nystagmus for about 30 min.
							0.5		+++	+	Nystagmus for about 30 min.; scalp EEG
W-6	CM						0.5		++		Vertical nystagmus for about 30 min.
W-7	CM	0.5		+							
		0.5		+							
W-9	CM	0.5	+	++	+(?)	Seizure soon after injection					
W-11	CM	0.5		++							
W-12	LV	0.5		++			0.5	+	+++		Seizure about 40 min. after injection
W-13	CM	0.5		++		EEG through implanted cortical electrodes	0.5		+++	+	EEG through implanted cortical electrodes
		0.5		++			0.5		+++	+	
W-14	CM	0.5		+							
46	CM	0.5		+			0.5		+++		

* CM, cisterna magna; LV, lateral ventricle.

† Docility: + indicates threatening behavior when approached; ++, no threatening and frightened behavior when approached, but monkey usually tries to escape or bite when handled; +++, no defensive behavior to rough handling, no danger of being bitten.

ing this stuporous episode frequently the EEG showed bursts of high-voltage multiple sharp and slow waves. The pattern of this burst activity was modified to a certain extent by noxious stimulus (Fig. 6). However, the appearance of this high-voltage burst activity always seemed to lag a little behind the actual onset of stuporous behavioral states. Sometimes this burst activity was not associated with this stuporous episode. The animal might be stuporous and unresponsive to various stimuli while the EEG was showing the typical arousal pattern (Fig. 7), indicating that the behavioral changes may not primarily be related to the mechanism of producing such EEG burst activity. The animal recovered from this episode very abruptly, with mewing, and showed remarkable flight and defense reaction, especially when a noxious stimulus was applied. About a week prior to the injection of the schizophrenic extract, the animal received the same amount of normal extract without producing such behavioral or EEG changes, although it became less active and less playful.

Table 1 lists the over-all effects of these extracts on cat behavior. The difference of effects of the two extracts is apparent. Schizophrenic extract induced a variety of peculiar behavioral patterns in 9 instances among 10 observations. Rage states were seen five times. No overlapping was seen between this rage state and other behavioral patterns.

Behavioral Changes in Monkeys.—Twelve monkeys were used for 21 observations (11 for normal extract; 10 for schizophrenic extract).

Table 2 lists the effects of intracisternal or intraventricular injection of each extract on monkey behavior. As seen in the Table, two significant behavioral changes occur. One is the remarkable docility, and the other is the range of peculiar behavioral patterns. The docility was seen in both extract groups, although its degree was much milder in the normal extract group.

As soon as the animals awoke from ether anesthesia, they ran about and climbed the cage wall quickly. They remained aggressive whenever approached. But within 20-30 minutes following the injection they gradually became expressionless, quiet, and less active. They no longer bared their teeth or showed threatening behavior when approached. When left undisturbed, they crouched in a comfortable position and tended to close their eyes, but they were readily aroused, even with a slight noise.

Those in the normal extract group usually lost their threatening or aggressive behavior but remained frightened. On the other hand, most of the schizophrenic extract group lost not only their threatening behavior but also their frightened behavior. They could be handled very roughly without inducing any wild defensive behavior (Fig. 8). During this period their climbing and walking became slow and slightly ataxic. Their extremities appeared to be hypotonic, but their muscle power was fairly well preserved, as shown by the fact that they can hang on to the experimenter's hand when pulled up.

The state of maximal docility lasted approximately 20-60 minutes after the injection. Subsequently, the monkeys became less docile and less ataxic. Although the animal became more active after the maximal docility, the tameness lasted more than 12 hours. When a lighted match was placed in front of one monkey's face (W-13), about seven hours after the injection, he blankly looked at the flame for a while and then started to lick it repeatedly, even after his whiskers had been singed and his tongue was in contact with the flame. Every time he touched the flame, he quickly withdrew his tongue, shaking his head and turning away from it. Then he calmly returned to the flame as though nothing had happened to him (Fig. 9). It seems obvious that this peculiar behavior is due to the loss of fear or to a disturbance of the learning and/or memory mechanism, despite the apparent preservation of sensory perception.

During the docile stage, three monkeys developed a generalized seizure. One occurred a few minutes after the injection of

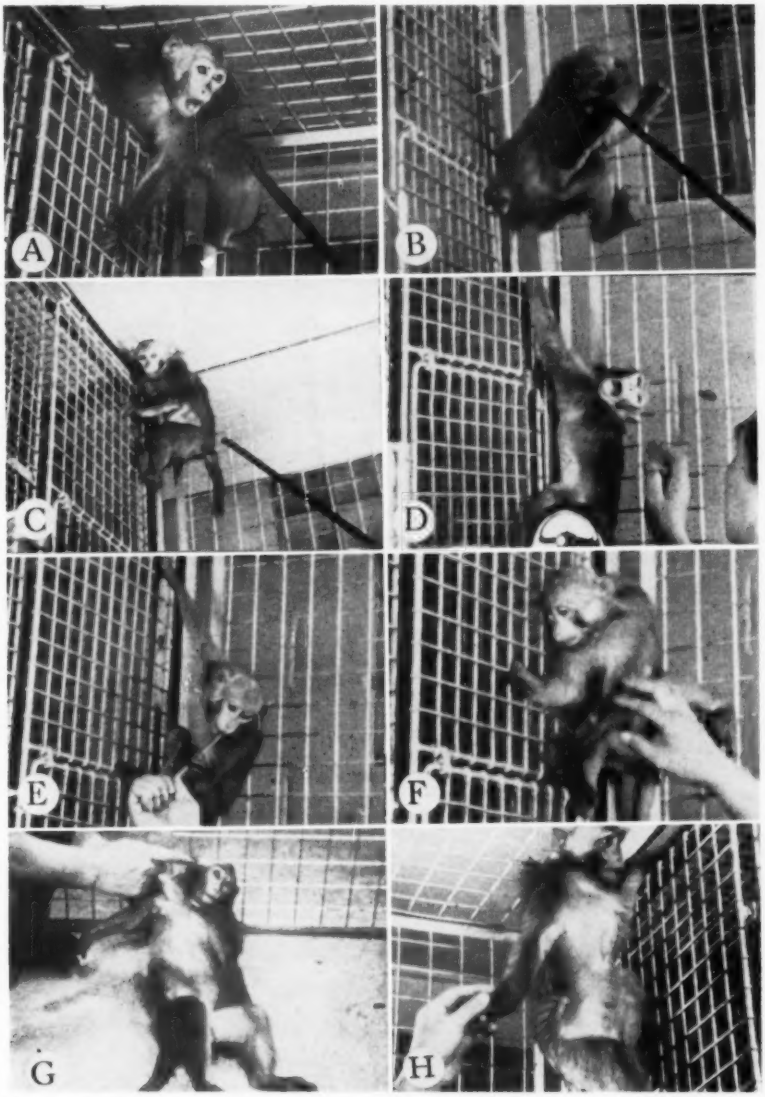


Fig. 8.—Docility following the intraventricular injections of 0.5 cc. of schizophrenic extract. (*A*) Before injection. (*B*) Ten (10) minutes after injection; animal still aggressive. (*C*) Fifteen (15) minutes; less aggressive. (*D*) Twenty (20) minutes; animal screams when approached. (*E*) Twenty-five (25) minutes; monkey tries to explore, without being frightened. (*F*) Thirty (30) minutes; no emotional response when approached. (*G*) Forty-five (45) minutes; monkey taken down to floor, does not struggle even when handled very roughly. (*H*) One hour; more active than before but remains tame.

normal extract (W-9, cisternal) but no particular change in the behavioral pattern was noted thereafter. It was in these latter two cases that a rather interesting observation was made. The seizures developed in these animals about 40 and 60 minutes, respectively, after the injection of schizophrenic extract (W-1, cisternal; W-12, ventricular), while the animals were at the height of their docility. When they recovered

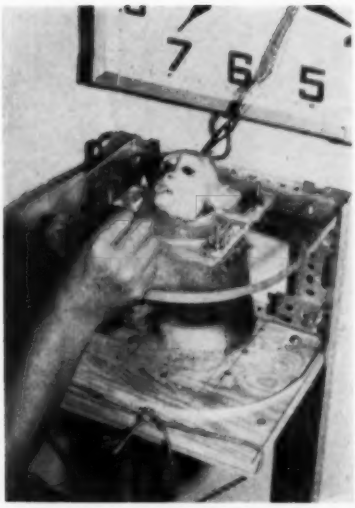
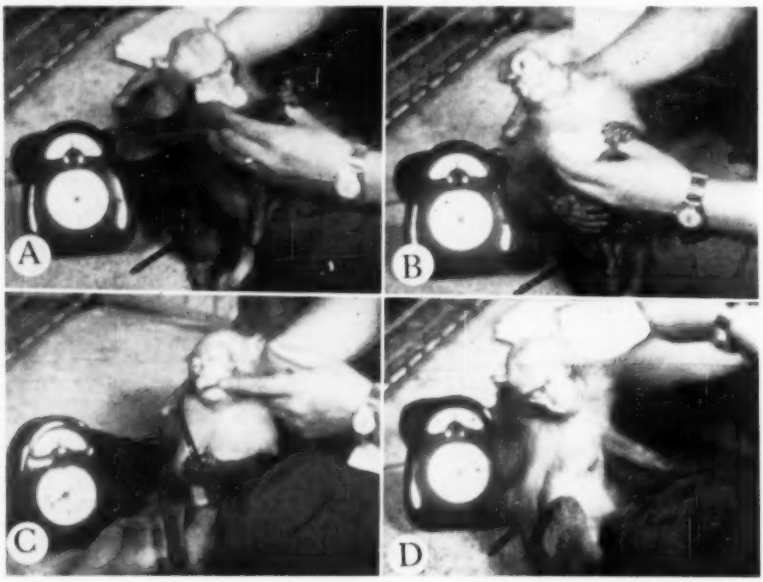


Fig. 9.—Monkey licking the lighted match about seven hours following the intracisternal injection of 0.5 cc. of schizophrenic extract.

from the seizure, to our surprise, they resumed almost normal behavior. They were no longer docile but attentive, alert, curious, and aggressive. They could no longer be touched without danger of being bitten. However, within the following hour they gradually became tamer and more docile again.

Following the initial docile stage, that is, about two to four hours after injection, some of the schizophrenic extract group (W-1, W-5, W-13) developed strange episodes, which are listed as "peculiar behavior" in Table 2. At first, it was found that these animals developed a peculiar episode, during which time they became unresponsive or inattentive. While the animal was eating an orange, he might stop eating suddenly and might become unresponsive to noxious stimulation (Fig. 10). When such an episode developed, after the animal had started eating a pellet, the monkey would stop chewing and hold the pellet in his mouth, the sequence of movement coming to a standstill (Fig. 11). Eating might begin again very abruptly, though the food had been held unmoved in the mouth for some time. The animal would eat peanuts at one moment, but not respond at all the next. During this period he did not respond to noxious, visual, or auditory

Fig. 10.—About two hours following the intraventricular injection of 0.5 cc. schizophrenic extract. (*A*) Animal eating orange; (*B*) stopped eating suddenly; (*C*) unresponsive; (*D*) no response to pinching of ear lobe.



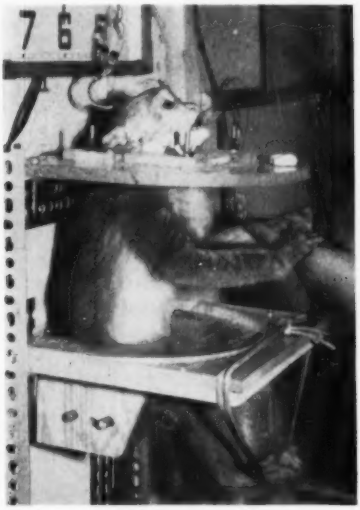


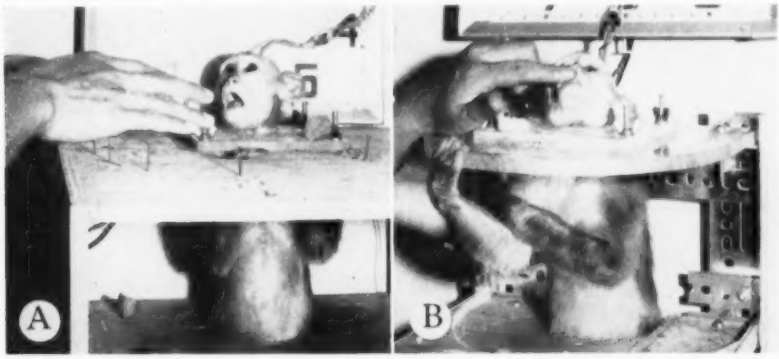
Fig. 11.—Stuporous episode about six hours after the intracisternal injection of 0.5 cc. of schizophrenic extract. Note the pellet in the mouth.

stimulation appropriately. There was often no response at all while intense noxious stimulation was applied to various parts of the body. Sometimes the monkey moved slowly when stimulation was applied and looked indifferently at the site pinched. He might try to touch the hemostat, indicating that the stimulation was perceived in some way, but he usually did not show any further concern. However, as soon as the episode was over, he became alert very abruptly and struggled and bit unless the stimulation was quickly withdrawn. During these "blank" episodes the animal did not resist, even when his mouth was forced open; the experimenter's hand was placed in the mouth without being bitten (Fig. 12). The animal held his hands up in the air and would maintain the given position as long as the episode lasted (Fig. 13). This position of the hands could be changed passively to some extent. As soon as the episode was over, he abruptly withdrew his hand and threw away the pencil which he had been holding during the episode. This has been well documented with colored moving pictures.

From the above description, it seems obvious that these episodes are due to the alteration of the conscious state, as signified by the variety of impaired reaction patterns. The duration of a single "blank" episode varied from a few seconds to a few minutes. The longest episode observed lasted approximately four minutes. This was repeatedly demonstrated up to 8 to 12 hours following the injection of schizophrenic extract. Usually the frequency and severity decreased as time passed.

These peculiar episodes were observed in three different monkeys, two of which (W-5 and W-13) reproduced exactly the same pattern on two different occasions, after receiving the same amount of the same schizophrenic extract. Thus, this episode was observed five times in three monkeys. Such peculiar episodes were not seen

Fig. 12.—(*A*) Before injection; monkey bellicose and noisy. (*B*) Stuporous episode; animal quiet and withdrawn.



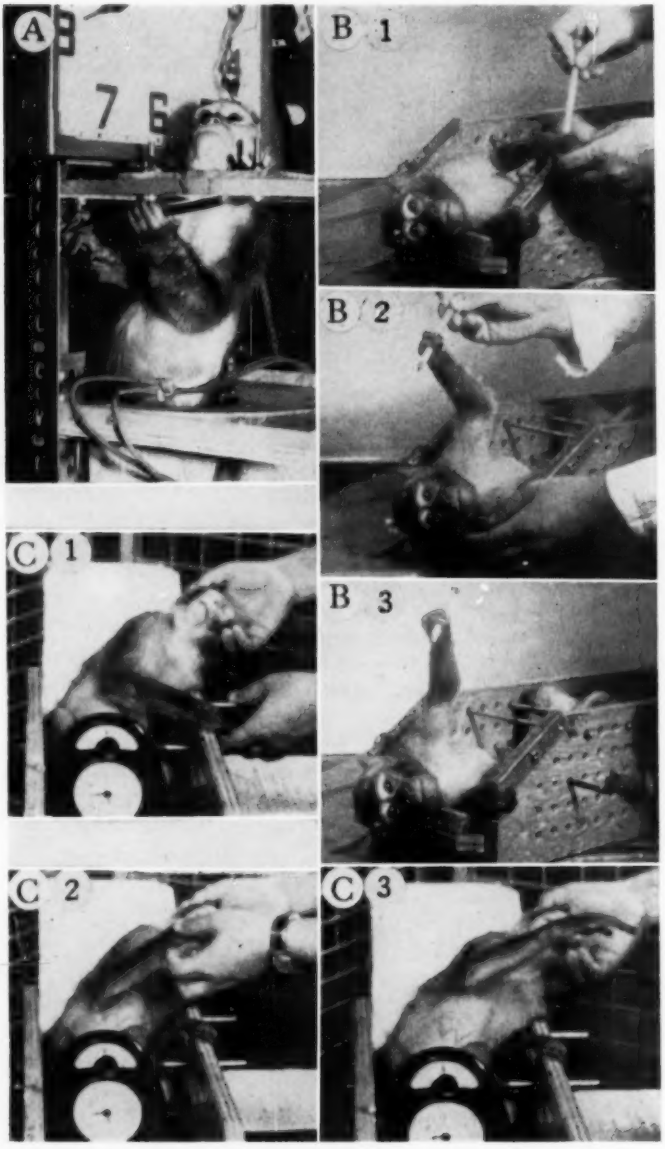


Fig. 13.—Stuporous episodes in three different monkeys following the injection of schizophrenic extract. (*A*) W-13; about eight hours. (This animal did not hold his hand in the air while he was sitting in the chair. However, as soon as the chair was rotated 90 degrees (lying position), he could hold his hand up in the air as long as the stuporous episode lasted.) (*B1, B2, C3*) W-1; about four hours. (*C1, C2, C3*) W-5; about six hours. Note the pencil in hands (*A* and *B*).

in the remaining five monkeys following the injection of the same schizophrenic extract. All of these three monkeys (W-5, W-13, W-1) were subjected to the normal extract injection but did not develop these peculiar episodes. Besides these peculiar episodes, sometimes these animals showed a strange behavioral pattern, which suggested that they were having some peculiar experience (Fig. 14).

Electroencephalographic recordings were made in two monkeys—one through implanted cortical electrodes, another through scalp electrodes during these behavioral observations.

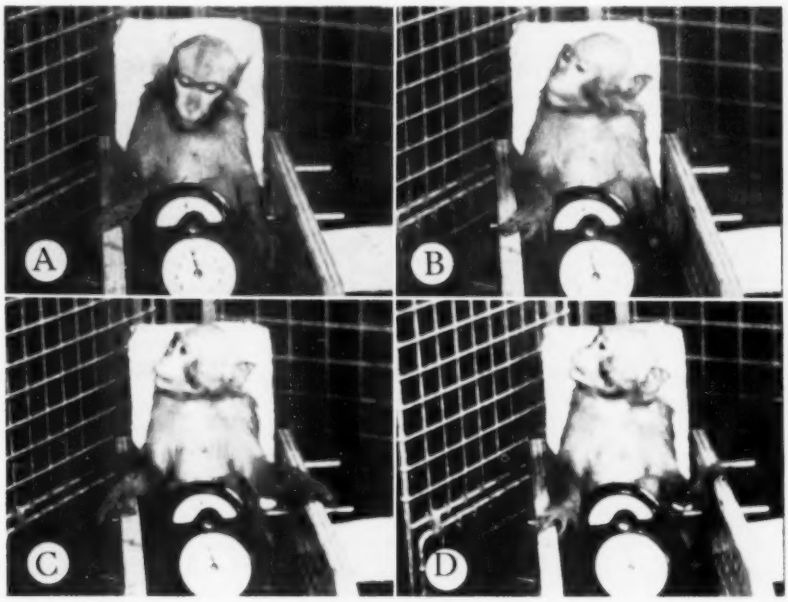


Fig. 14.—About 12 hours after intraventricular injection of 0.5 cc. of schizophrenic extract. While monkey was sitting quietly (*A*), he suddenly looked to the right (*B*), as though hearing something (*C*), despite the fact that the laboratory was completely quiet. He remained in this attitude for about 30 seconds (*D*).

Before the injection of the schizophrenic extract, the EEG showed an immediate and lasting activation pattern, characterized by low-voltage fast activity set off by even a slight noise or movement of the experimenter in the laboratory. After the animal had developed a typical docile state, the activation pattern was less easily obtained unless noxious stimulation was applied. The pain stimulation usually produced immediate behavioral as well as electroencephalographic arousal, but its duration was extremely

Fig. 15.—Electroencephalogram of monkey recorded through scalp electrodes. (*A*) Before injection. Slight noise (arrow) in the laboratory caused immediate arousal pattern. (*B*) Two hours after intraventricular injection of 0.5 cc. of schizophrenic extract. Monkey is very docile. Black bar indicates touching animal's hand. The arrow indicates pinching of hand.

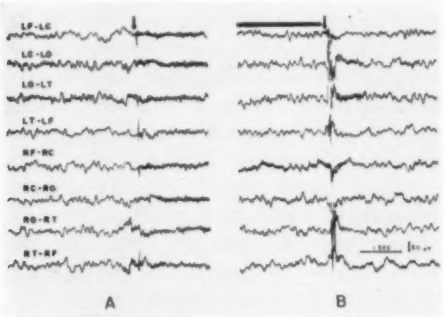
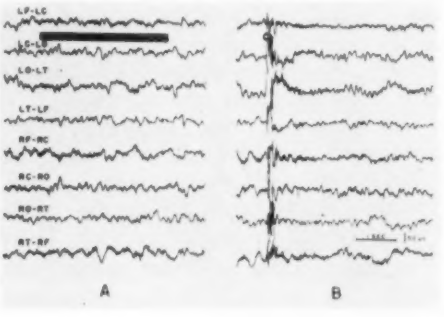


Fig. 16.—Electroencephalogram of monkey recorded through scalp electrodes, about three hours following the intraventricular injection of 0.5 cc. of schizophrenic extract. (*A*) No behavioral response to the pinching of cheek (black bar) during stuporous episode. (*B*) Animal is docile but not stuporous. Pinching of ear lobe (*a*) induced an immediate defensive movement.



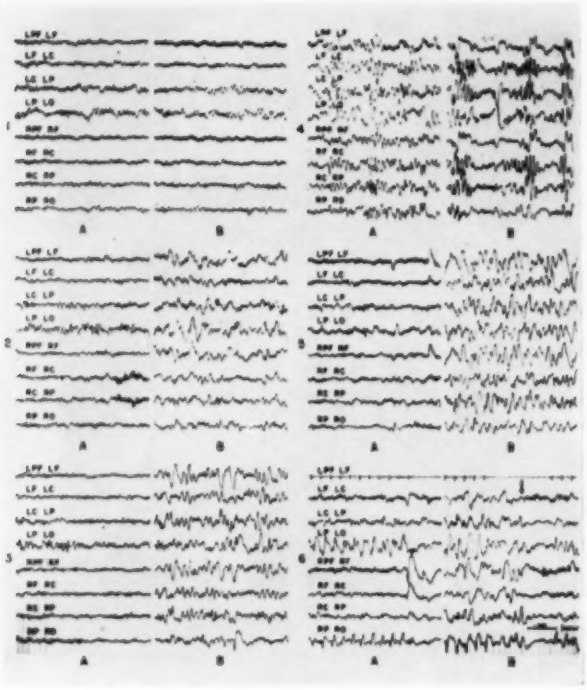


Fig. 17. — Electroencephalogram of monkey following the intracisternal injection of 0.5 cc. of normal and schizophrenic extracts. The same monkey with implanted electrodes was used twice. Records following the normal extract are represented by (*A*) and the schizophrenic extract, by (*B*). *A* was taken about 10 days after *B*. (*1*) Normal control. (*2*) Thirty (30) minutes; animal is developing docility. (*3*) Three (3) hours: (*A*) animal docile but alert; (*B*) stuporous episode. (*4*) Three (3) hours: (*A*) light sleep; (*B*) stuporous episode, animal's eyes are widely open. (*5*) Six (6) hours: (*A*) animal docile but awake; (*B*) stuporous episode. (*6*) Eight (8) hours: photic stimulation (Channel 1 is connected to photo cell); arrow in (*B*) indicates that animal became alert. Note the reduction in amplitude of photic response on recovering from stuporous episode.

short (Fig. 15). However, during the stuporous episodes mentioned above, even an intense and lasting pain stimulation frequently failed to produce a full activation pattern (Fig. 16). At the beginning of the pain stimulation the record might flatten to some extent, but preexisting slow waves soon returned, even when the stimulation of the constant intensity was applied. Frequently during the stuporous episode high-voltage irregular slow-wave discharge was seen over all the recording sites. Also, occasional bilateral synchronous high-voltage 6-8 cps burst activity, similar to that of the typical light-sleep pattern, developed during the episode, although the animal's eyes might be widely open (Fig. 17, *4B*). Again, as in the cat, the appearance of this burst activity seemed to have some lag following the onset of behavioral changes. However, this was by no means the specific pattern of a stuporous episode. There were many similar episodes without any concomitant changes in background activity before, during, or after the episode. Sometimes noxious stimulation produced faster activity without making the animal alert. At another time there were no visible changes in background activity. Therefore, no identification of this "blank" episode could be made made by the electrographic pattern alone.

The spike discharge, which was seen in some cats after the injection of schizophrenic extract, was not observed in this limited number of monkeys. After the animals developed a docile state, there was definite increase in 2-5 cps slower waves in the background activity, instead of the 6-8 cps rhythmic pattern, as found in normal conditions. This generalized slowing disappeared about 48 hours after the injection of schizophrenic extract.

In the normal extract group, 11 observations were made on 9 monkeys, and no "blank" episode developed, except in one. This monkey (W-9) received the comparable doses of normal extract into the cis-

terna magna. About five hours later he developed a peculiar state, during which time he no longer responded to the rough handling. However, this unresponsive state was interrupted immediately after a hand clap was given, within a minute after it began, and this state was never observed again during nine hours of observation. There were no significant abnormalities in EEG pattern after the injection of normal extract in two monkeys (Fig. 17, *A*). Although the record showed a frequent occurrence of drowsy patterns when undisturbed, this was promptly replaced by low-voltage fast activity after touching the animal, or after whistling or moving about by the experimenter. Pinching the body during the drowsy state produced immediate arousal pattern, accompanied with the active defense movement. However, the over-all duration of the low-voltage fast activation pattern was considerably diminished.

Comment

The schizophrenic urine extract produced a variety of unusual behavioral changes, which have never been seen in the normal extract group. The rage state and the automatism-like behavior were observed only in cats. There was no superimposition of the rage state and the automatism-like behavior in the same cat. The electroencephalogram in the latter showed concomitant high-voltage, sharp wave-and-spike discharges in the temporo-occipital area. Recurrent stuporous episodes were observed in three monkeys and one cat. The reason for the development of certain unusual behavior in only a limited number of animals is unknown.

The difference in the behavioral effects between cat and monkey following injection of the schizophrenic urine extract is striking: the marked docility in the monkey and the rage state in the cat. This finding is not too surprising from the point of view of the similar-species discrepancy in the behavioral effects following bilateral removal of pyriform-amygdalohippocampal region.[4,22]

A number of workers have reported that they have produced bizarre behavioral changes in animals resembling human catatonic stupor following destructive lesions in the brain,[3,18] intraventricular injection,[7,31] and intravenous injection of certain drugs.[19,20] On the basis of the sometimes very striking similarity between intraventricular drug effects and effects of localized stimulation and lesions in the brain, Sherwood[35] states that the effects induced by intraventricular drug injection are likely due to central selective toxicity, not peripherally mediated, along the accessible anatomical structures in the vicinity of the third and fourth ventricles. Destruction[9] or stimulation[14,15,17] of this periventricular mass readily produces a variety of changes in adaptability, awareness, and consciousness, as well as in autonomic and vital functions. Complete or partial loss of appropriate responses to external stimuli during the "blank" episodes, following the intraventricular or cisternal injection of schizophrenic urine extract, suggests the possibility that the schizophrenic urine extract exerts its toxic effect on the central core of subcortical gray matter.

In recent years the functional organization of the reticular neuronal system of brain stem has been studied extensively. Its direct stimulation desynchronizes the EEG in a manner simulating awakening from sleep or alerting to attention. Collaterals from all afferent paths to the cortex turn into this subcortical system and EEG arousal induced by afferent stimulation can be shown to be mediated through it. Injury to its cephalic portion leads to chronic loss of wakefulness. Reversible pharmacologic block of its ascending influences upon the hemisphere may provide a neural basis for the anesthetic state.[26]

During the "blank" episode following the schizophrenic urine extract our animals could not be aroused behaviorally, although evoked cortical responses were readily recorded during this period. This suggests that the functional alterations of the reticular activating system was the likely underlying cause. Variations in the modification of EEG and behavioral pattern following

sensory stimulation, ranging from complete loss of response to partial arousal, further suggest gradations in functional alteration of this system during these episodes.

Certain similarities are present between the "blank" episode following the injection of schizophrenic urine extract and "inhibitory" symptoms—such as reduction of emotional expression, apathy, "arrest" or "freezing" of activity, loss of contact with environment—due to seizure discharge in the rhinencephalic system.[2,5,16,21,33] In view of the recurrent appearance and very abrupt onset and end of "blank" episode, the possibility of recurrent ictal discharge within responsible subcortical structures cannot be excluded. The electrical events occurring in depths are not necessarily reflected on the surface activity.[1,36]

Recent electrophysiological evidence suggests that the rhinencephalon is a pool into which afferent impulses of all kinds of modalities enter,[12] and that the amygdala, and perhaps also other parts of the rhinencephalon, act as a modulator of complex mechanisms integrated in the central core of subcortical structures extending from septum through hypothalamus into brainstem tegmentum.[11] During the stuporous episodes there was no characteristic set of electroencephalographic patterns. Frequently the typical electroencephalographic arousal pattern was induced without accompanying behavioral arousal. Also, bilateral high-voltage slow-wave-and-spindle burst activity developed during the episode, but the appearance of the former always lagged somewhat behind the onset of the behavioral episode. These findings seem to suggest that the postulated functional alteration of brainstem arousal mechanism may well be secondary to some other modulating mechanism closely associated with it.

Although the normal urine extract did not produce any unusual behavioral changes in the animals, as did the schizophrenic urine extract, both extracts exerted a marked taming effect in monkeys. Whether the taming mechanism is directly related to the peculiar behavioral pattern following the injection of schizophrenic extract is not clear. From the view held by many workers that the rhinencephalon plays an important role in emotional behavior,[27,29,31] it is tempting to correlate the possible functional alteration of this system with the significantly modified and reduced emotional coloring following these extract injections. If this is the case, the difference observed in the over-all effects following the schizophrenic and the normal urine extract injection might well be quantitative. However, it must be recognized that evidence is as yet insufficient to permit one to state whether this difference is qualitative or quantitative.

Summary

Two urine extracts derived from a group of acute schizophrenic patients and from a group of normal subjects were injected into either the cisterna magna or the lateral ventricle of cats and monkeys, and their effects on the animals' behavior and the electroencephalogram in some animals were studied.

Following injection of the normal extract, cats became less active but remained affectionate. Schizophrenic extract caused more pronounced reduction in spontaneous activity, and no affectionate response was obtained, even when the animal was caressed. In monkeys both extracts caused a marked docility, with significant reduction in emotional coloring of their behavior. The degree of this change was more pronounced following the schizophrenic extract.

Schizophrenic extract brought about varieties of unusual behavioral patterns, ranging from rage states (5 out of 10 cats), automatism-like states (3 out of 10 cats) to recurrent stuporous and catalepsy-like episodes (1 of 10 cats, 5 of 10 monkeys). No animal, after injection of the normal extract, showed this unusual behavior, except for a brief stuporous episode in one monkey.

Electroencephalograms were recorded in some animals through implanted cortical electrodes, and also from scalp electrodes. No significant abnormality was noted after the normal extract injection except for the

frequent occurrence of a drowsy pattern. Following the injection of schizophrenic extract, predominance of 2-5 cps slow waves in background activity was observed. Paroxysmal high-voltage sharp-wave-and-spike discharges occurring at temporo-occipital regions were associated with the automatism-like behavior in two cats. While the animals' eyes were kept widely open during the stuporous episodes, the electroencephalogram frequently showed high-voltage slow-wave-and-spindle burst activity bilaterally. In some episodes the electroencephalogram showed a low-voltage fast "arousal pattern," despite the fact that animals remained unresponsive. Evoked potentials in response to sensory stimulation were recorded during this period.

Possible implications and mechanisms of the present behavioral and electroencephalographic findings are discussed.

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Perception of Reversible Figures After Brain Injury

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Reversible figures are drawings in which figure and ground appear to alternate on continued inspection (e. g., the Rubin vase, Fig. 1*A*), or in which perspective appears to shift (e. g., the Necker cube, Fig. 1*B*); in yet a third type, a moving pattern, such as the vanes of a windmill, seems to reverse the direction of its movement. The neural mechanisms underlying these apparent fluctuations remain obscure, despite numerous investigations involving such aspects of the patterns as size (Washburn, Mallay, and Naylor[34]; Cohen[5]), "complexity" (Donahue and Griffitts[7]; Washburn, Reagan, and Thurston[35]), or brightness (Mull, Ord, and Locke[19]).

That retrochiasmal processes are involved, however, is suggested by two facts: (*a*) In figures with reversible perspective or movement, rate of apparent change (RAC) increases with continued fixation (Köhler[15]; Brown[3]; Cohen[5]), and (*b*) inspection of a reversible figure with one eye causes an increased RAC of the same figure when it is subsequently viewed with the other eye (Brown[3]). Such general factors as fatigue cannot be considered responsible for the increased rate, since prior inspection of a homogeneous field (Brown[3]; Cohen[5]) or of dissimilar patterns (Cohen[5]) does not result in increased RAC. Similarly, peripheral factors, such as ocular movements, cannot account for either the phenomenon of figure reversal itself or the increase in figure reversal with continued inspection: Monocular fixation between two reversible figures often results in asynchronous, "out-of-phase," fluctuations (Washburn, Mallay, and Naylor[34]).

Of special interest in this connection are several reports that the number of reversals is reduced following brain damage. The earliest reports dealt exclusively with figure-ground reversal (in contrast to perspective fluctuation) and did not attempt to localize the cerebral lesions. Goldstein and Scheerer[11] suggested that persons who have incurred brain damage often become "rigid" in their performance. As a consequence, "if confronted with the ambiguous figures of Rubin, they will at best recognize one aspect, the face or the vase, but are unable to shift from one aspect to the other." Elsewhere, however, Goldstein[10] reported that brain injury may result "in the instability of the figure, and therefore in a tendency to inversion of figure and ground." Thus, brain injury could result in either too many or too few reversals; no criteria were offered to predict the consequences in a specific case.

Harrower[12] tested 30 subjects with brain tumors and 30 controls, using Rubin's face-vase figure, together with six modifications of this figure. Three of these modifications were drawn so that the "faces" aspect was most prominent; the other three figures emphasized the "vase" aspect. Harrower found that normal controls saw the appro-

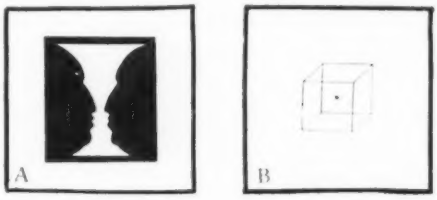

Fig. 1.—Rubin Vase and Necker Cube.

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Dr. H. L. Teuber, Director of the Psychophysiological Laboratory, assisted in all phases of the present investigation.

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priate modified figures as faces or vase, and gave mixed reports for the ambiguous midpoint (Rubin's original figure). The brain-injured group differed from the normal controls in four ways:

(*a*) They perseverated throughout the series with their original perception.

(*b*) They failed to recognize the ambiguous figure as a meaningful object.

(*c*) They were unable to see the less dominant figure at will.

(*d*) They perceived new objects instead of the vase or faces.

These findings were interpreted in Goldstein's terms as a deficit in "spontaneous sensory organization" and a "loss of abstract attitude."

Subsequent investigations were concerned primarily with attempts to demonstrate that the frontal lobes are uniquely concerned with perception of reversals; these studies employed figures with ambiguous perspective, as well as those with ambiguous figure-ground relations. Yacorzynski and his associates[36] reported that five patients with unilateral frontal-tumor resection either showed a markedly reduced RAC or failed to see reversals in a number of ambiguous patterns, while one psychiatric patient tested before and after bifrontal lobotomy showed no change of reversal rate. These authors concluded that destruction of frontal cortex, rather than subcortical fiber tracts, was necessary to produce the "frontal-lobe sign" of decreased reversal rate.

More recently, Feinberg[9] studied Necker-cube reversal in 12 men with penetrating frontal-lobe injury and 40 controls without brain injury. He employed Necker cubes of different sizes; to half of each group the cubes were presented in order of decreasing size, and to the other half, in reverse order. The brain-injured who viewed the large cubes first reported fewer reversals than did the controls or brain-injured subjects who were tested with cubes in the order of increasing size. Feinberg concluded that frontal-lobe lesions reduce reversal rate under the special condition of presenting first larger and then smaller cubes.

These investigations have serious limitations, which could have been avoided by using additional controls. In Feinberg's study, five of the six patients with frontal-lobe lesions tested with stimuli in descending order had unilateral lesion, while five of the remaining six with frontal-lobe lesions tested with stimuli in ascending order had bilateral lesions; factors of laterality of lesion and order of stimulus presentation were thus confounded. Similarly, frontal lobotomy is a bilateral procedure, whereas lowered RAC was observed only in the group with unilateral tumor resection. These findings (Yacorzynski, Boshes, and Davis[36]; Feinberg[9]) may therefore indicate that RAC is altered only by unilateral, and not by bilateral, injury.*

Of greater importance is the failure of any of these studies to employ a non-frontal-brain-injured control group: obviously, the designation of reduced or increased RAC as a "frontal-lobe sign" may be unwarranted, since injury to *any* area of the brain may have been sufficient to alter reversal rate. Petrie, in a recent study, has in fact observed reduced Necker-cube reversals after unilateral resection of the temporal lobe (Petrie and Orchinik[23]).

* The suspicion that bilateral frontal lesions may produce effects on RAC different from those of unilateral damage to these structures is enhanced by the reports of Petrie.[23] She noted some increase in Necker-cube reversals following bifrontal lobotomy, when preoperative scores (total reversals for one-minute observation periods) were compared with corresponding scores obtained three months postoperatively. The postoperative increase, however, was significant only under the special condition of "willed" reversals, i. e., when the patient was instructed to see as many reversals as possible (Petrie[23]). Moreover, the increased reversal rate was nonsignificant when patients with anterior frontal lobotomies were retested nine months (rather than three months) after the operation. The findings by Petrie nevertheless suggest that bilateral frontal lesions should be compared with those restricted to one frontal lobe, and with unilateral and bilateral lesions involving other lobes of the brain.

The present investigation was therefore undertaken to answer the following questions: (*a*) Does brain injury alter RAC; and, if so, is such change selective for frontal lesion? (*b*) What are the effects of unilateral *vs.* bilateral injuries on RAC? (*c*) In men with unilateral injuries, is RAC differentially affected in the ipsilateral and contralateral halves of the visual field relative to the side of injury? Figure-ground reversal (Rubin vase) and perspective reversal (Necker cube) may be mediated by different processes; in the interest of simplicity, the present report will deal only with perspective reversal.

Methods and Materials

Subjects.—Fifty-four nonhospitalized men with penetrating missile wounds of the brain—veterans, for the most part, of World War II—served voluntarily as experimental Ss. Twenty-one veterans with peripheral nerve injuries, also nonhospitalized volunteers, served as controls. All Ss were drawn from the roster of the Psychophysiological Laboratory, New York University College of Medicine. Wounds of entrance and of exit, if any, as well as sites of retained foreign bodies, were determined by review of surgical records and x-rays, and were charted on standard skull and brain diagrams. Each case was then classified according to whether he had damage to either or both hemispheres, and whether in the frontal, parietal, temporal, or occipital lobe, or in combinations of these. In this fashion, cases were designated as having, e. g., left frontoparietal, bilateral frontal, or right temporo-occipital lesions. These localization procedures had been carried out prior to the present study, for all cases tested at the Psychophysiological Laboratory.

The classification was based solely on known penetration, and no estimates of the mass of tissue destroyed were attempted. Thus, locus designations refer only to approximate areas of minimal involvement, and may be an underestimation of actual damage. However, these limitations with regard to localization are presumably equal for the various subgroups established in the brain-injured population.†

† Dr. H. L. Teuber and his associates in the Psychophysiological Laboratory, especially Drs. Josephine Semmes and S. Weinstein, granted permission to use their classifications according to locus of lesion, their sensorimotor and visual-field data, and other collateral information on the cases on which this report is based.

Visual fields of all brain-injured Ss were determined by routine perimetry, and in some cases by more detailed campimetric examination. Most, but not all, Ss were tested with the Army General Classification Test, First Civilian Edition (AGCT), as part of a larger study of intellectual change following brain injury (Weinstein and Teuber[33]; Teuber and Weinstein[31]).

The selection of brain-injured Ss was based on the following criteria: (*a*) the numbers of cases with left- or right-hemisphere lesions for each lobe injured were balanced as far as possible; (*b*) all "bilateral" cases had injury bilaterally in at least one lobe; e. g., a man with injury to the left frontal and right parietal lobes would have been excluded, whereas a man with left frontal and right frontoparietal lesions would be included; (*c*) Ss were excluded who had large or centrally located scotomata which tended to obscure any portion of the stimulus figures. Actually, only one S with a field defect (Case 64) was included; he had moderate bitemporal constriction of the visual fields.

Stimulus Figures and Testing Conditions.—The test figure was a double Necker cube (Fig. 2), presented in three sizes, the lengths of one side being 0.7, 1.6, and 4.9 cm., respectively. This figure was used because simultaneous bilateral presentation (Oppenheim[20]; Bender[1]; Bender and Teuber[2]) often reveals unilateral dysfunction in men who show no abnormality on unilateral stimulation; it was thus hoped that this bilaterally symmetrical figure, when centrally fixated, might also reveal unilateral deficits which otherwise would be missed.

Stimulus figures were mounted vertically on a table in S's frontal plane against a homogeneous background. Illumination was provided by a 15-watt Standard Cool White fluorescent lamp. For half the Ss, figures were illuminated from the left; for the other half, from the right. The response-recording apparatus consisted of a box with two buttons on its upper surface, each of which actuated its own counter. Ss were instructed to fixate the small horizontal bar on the vertical border shared by the two cubes; they were asked to respond to shifts in apparent perspective of

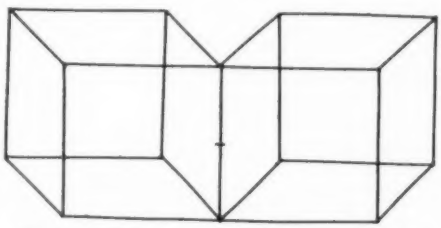

Fig. 2.—Double-cube stimulus patterns employed in testing all subjects.

either the left or the right half of the double cube by pressing the left or the right button, respectively, and to press both buttons if both halves of the figure appeared to shift together.

Experimental Design.—Each of the three sizes of the double cube was presented twice, in the following order: large—middle—small—small—middle—large; the presentations lasted 90 seconds, followed by rest periods of 3 minutes, so that the total testing session, for each S, was 24 minutes. The following variables were taken into account.

(*a*) Conditions: For purposes of analysis, the first three presentations (large—middle—small) were designated as Condition I; the next three (small—middle—large), as Condition II.

(*b*) Observation Periods (OPs): To evaluate changes in RAC during shorter periods of continuous observation, each 90-second presentation was subdivided into six 15-second OPs. The number of reversals reported for one 15-second OP for one of the cubes, left or right (see below), constituted the smallest unit of analysis.

(*c*) Sides: For all Ss with unilateral lesion, the half of the visual field on the side of the injured hemisphere was called "ipsilateral"; the half-field opposite the injured hemisphere was called "contralateral." Men with bilateral injuries were excluded from analyses involving the "sides" variable. For half the controls, the left half-field was arbitrarily designated "ipsilateral"; for the remaining half, the right half-field was designated "ipsilateral."

(*d*) Groups: The brain-injured population was subdivided into the following groups: frontal (all Ss with unilateral injury involving the frontal lobe) *vs.* nonfrontal (remaining Ss with unilateral lesion sparing the frontal lobe); and, analogously, parietal *vs.* nonparietal; temporal *vs.* nontemporal; occipital *vs.* nonoccipital; left *vs.* right (all Ss with lesions restricted to the left or the right hemisphere, respectively). In the analyses in which the role of frontal and parietal lesions was considered and the contribution of "sides" excluded, groups with bilateral injury were considered as well as those with unilateral injury. In the analysis comparing left- and right-hemisphere lesions, as well as bilateral penetration, the bilateral group comprised all cases in which lesions were known to have encroached on both hemispheres.

Analysis of Data.—The data were analyzed by three series of three-factor analyses of variance, each series differing in the choice of variables considered together. These series were (*a*) group×condition×OP; (*b*) group×side×condition, and (*c*) group×side×OP. Each of these series consisted of five separate analyses, differing only in the manner in which the brain-injured population was classified. Significant results of *F*-tests in the analyses of variance indicated that the distribution of scores among the categories of a given variable was unlikely to occur by chance. These were followed by appropriate *t*-tests to determine the significance of differences between specific categories of such variables.‡

‡ Dr. Leonard Kogan acted as statistical consultant to the Psychophysiological Laboratory and devised the statistical procedures employed in this study.

TABLE 1.—*Summary (Values for F)* of Analyses of Variance†*

Series (*a*): Group×Condition×Observation Period						Series (*b*): Group×Condition×Side ‡		
Source	Frontal Analysis	Parietal Analysis	Temporal Analysis	Occipital Analysis	Laterality Analysis	Source	Frontal Analysis	Temporal Analysis
Groups	3.44 §	2.55 §	1.61	2.24	3.49 §	Groups	2.64	1.64
Conditions	51.20 ‖	51.72 ‖	45.29 ‖	44.26 ‖	51.15 ‖	Sides	—	—
OPs	21.11 ‖	21.89 ‖	21.12 ‖	21.33 ‖	21.25 ‖	Conditions	44.27 ‖	44.83 ‖
Condition×OP	4.56 ¶	4.05 ¶	2.67 §	4.15 ¶	4.32 ‖	Side×Condition	1.51	—
Group×Condition	—	1.31	—	3.60	4.67	Group×Side	—	—
Group×OP	1.52	1.85 §	2.23 §	2.54 ¶	1.85 §	Group×Condition	—	—
Group×Condition×OP	1.72 §	—	1.14	—	—	Group×Side×Cond.	5.69 ¶	11.09 ‖
Groups (N)								
Control	21	21	21	21	21		21	21
Unilateral	F 19	P 19	T 13	O 6	Right 18		F 19	T 13
Unilateral (non)	Non-F 20	Non-P 20	Non-T 26	Non-O 33	Left 21		Non-F 20	Non-T 26
Bilateral	F 10	P 6						
Bilateral (non)	Non-F 4	Non-P 7						

* Significance of *F*-values refers to tests using appropriate error or significant higher interaction terms.

† Only Series (*a*) and (*b*) summarized. The unique contribution of Series (*c*), i. e., the Group×Side×OP interaction failed to reach significance in any analysis.

‡ Except for the Frontal and Temporal Analyses shown, "Groups," either as a main effect or in interaction with other variables, failed to reach statistical significance.

§ $P<0.05$.

‖ $P<0.001$.

¶ $P<0.01$.

TABLE 2.*—*Average Total Reversals: Frontal and Parietal Analyses*

Mean	Frontal Analysis Subgroup		Mean	Parietal Analysis Subgroup	
227.50	Bilateral frontal	$P<0.001$	224.14	Bilateral nonparietal	$P<0.05$
183.48	Control	$P<0.01$	189.50	Bilateral parietal	
166.55	Unilateral nonfrontal		183.48	Control	
166.50	Bilateral nonfrontal	$P<0.02$	164.40	Unilateral parietal	$P<0.05$
132.63	Unilateral frontal		136.20	Unilateral nonparietal	
	Groups (N):			Groups (N):	
	Control (21)			Control (21)	
	Uni-F (19)			Uni-P (19)	
	Bil-F (10)			Uni-Non-P (20)	
	Uni-Non-F (20)			Bil-P (6)	
	Bil-Non-F (4)			Bil-Non-P (7)	

* Based on significant F for Groups in Frontal and Parietal analyses; $P<0.05$.

Results

General Results.—The principal results of the analyses of variance, Series (*a*) and (*b*), as described in the preceding section, are summarized in Table 1.

Effects of Frontal Injury.—When the average total numbers of reversals reported by the subgroups in the frontal-lobe analysis were listed in order of descending magnitude, and lines drawn between adjacent groups differing significantly from one another (Table 2), a fairly clear result emerged: Bilateral frontal lesion led to a significant increase of reversal rate, while unilateral frontal lesion produced a significantly decreased reversal rate. Nonfrontal lesions, unilateral as well as bilateral, caused a significant but smaller reduction in total reversals.

Other deficits became apparent when reversal rate was considered a joint function of frontal injury and continuous observation § (Fig. 3). While the maximum RAC was significantly lower and was reached significantly earlier by both unilateral frontal and nonfrontal groups, only the unilateral frontal group showed a decreased initial RAC.

§ Group×OP interaction of frontal analysis in Series (*a*) significant; $P<0.01$.

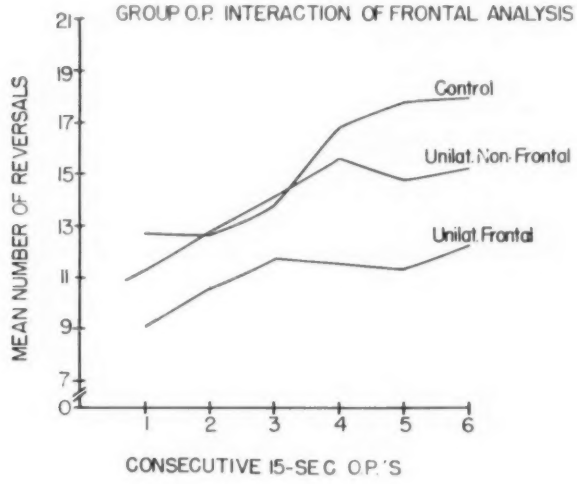

Fig. 3.—Rate of apparent change as a function of frontal lesion×observation period.

TABLE 3.—*Average Total Reversals: Parietal Injury With and Without Frontal Involvement*

Group	Mean	N
Control	189.5	21
Unilateral parietal and frontal lobe	109.2	6
Unilateral parietal without frontal lobe	190.2	13
Bilateral parietal and bilateral frontal	235.3	3
Bilateral parietal without bilateral frontal	143.7	3

Another change was found when RAC was considered a joint function of frontal injury, side of the visual field, and prolonged testing.‖ Under Condition I, ipsilateral and contralateral lesions did not differ from one another for the control, unilateral frontal, and nonfrontal groups. During the second half of testing (Condition II), both brain-injured subgroups showed a significantly smaller increase in the contralateral half of the visual field than in the ipsilateral side ($P<0.001$). This lateral disparity was most pronounced in the nonfrontal group.

To determine whether the deviations of total RAC of the bilateral and unilateral frontal groups could somehow have been secondary to differential impairment of psychometric intelligence, correlation coefficients (Pearson's r) were computed between total reversal and AGCT raw scores for those men whose AGCT scores were available. These were −0.19 for the controls, +0.24 for the bilateral frontal group, and −0.44 for the unilateral frontal group. None of these correlation coefficients reached significance.

Effects of Parietal Injury.—The results of analysis of the parietal group (Table 3) may best be understood by considering the consequences of the "complementary" method of subdividing the experimental population. Since our brain-injured group contained no cases of bilateral temporal lesion, and only one instance of bilateral occipital injury (in which there was also bilateral parietal involvement), the bilateral nonparietal group was composed entirely of men with bilateral frontal injuries. This fact alone was sufficient to account for the high mean RAC of this group. The curious finding that the bilateral parietal group had a higher mean than the controls reflects the fact that three of the six bilateral parietal cases also had bilateral frontal injury. Comparison of those men who had bilateral parietal *plus* bilateral frontal lesion with those Ss who had bilateral parietal but did not have frontal involvement showed that the bilateral frontal cases accounted for the high bilateral parietal group mean (Table 3). Similarly, the unilateral parietal group was approximately equivalent to the unilateral nonfrontal group, and the unilateral nonparietal group, to the unilateral frontal group. Thus, parietal lesion produced few distinctive defects which could not be traced to concomitant frontal involvement: Unilateral, as well as bilateral, parietal lesions led to moderate reduction in reversal rates. By contrast, unilateral frontal lesions led to marked reduction, and bilateral frontal lesions, to marked enhancement of reversal rates.

‖ Group×Condition×Side interaction of frontal analysis in Series (*b*) significant; $P<0.01$.

TABLE 4.*—*Average Reversals Ipsilateral and Contralateral to Injured Hemisphere in Conditions I and II: Temporal Analysis*

		Condition I	Condition II
Controls N-21	Ipsi-	40.57	50.48
	Contra-	41.71	50.71
Temporals N-13	Ipsi-	30.46	39.85
	Contra-	33.23	38.08
Nontemporals N-26	Ipsi-	33.50	45.85
	Contra-	31.85	43.04

* Based on significant Group×Condition×Side interaction in Temporal analysis, Series (*b*); $P<0.001$.

Effects of Temporal Injury.—The most striking effects of temporal lobe injury were seen on initial, and after prolonged, testing (Table 4); the initial rate ipsilateral to the injured hemisphere was remarkably low as compared with controls ($P<0.01$), and there was much less than the normal increase of RAC in the contralateral halffield in Condition II.

Effects of Occipital Lesion.—When occipital lesion was considered together with continuous observation,¶ unilateral lesion

¶ Based on significant Group×OP interaction, occipital analysis, Series (*a*); $P<0.01$.

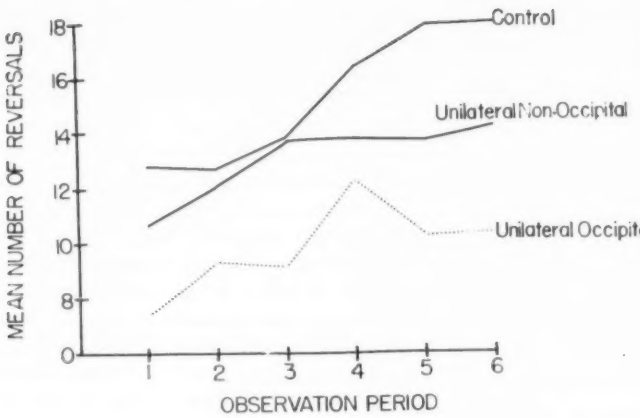

Fig. 4.—Rate of apparent change as a function of occipital lesion×observation period.

was seen to result in an altered time course of reversal rate which was strikingly similar to that of the unilateral frontal group (Fig. 4; cf. Fig. 3). However, occipital lesion did not significantly reduce the total number of reversals, nor were there differential effects after prolonged testing or on either side of the visual field. In this respect, occipital and frontal injuries differed.

Effects of Laterality of Lesion.—Men with right-hemisphere lesions reported significantly fewer total reversals than did Ss with bilateral injuries ($P<0.01$) or controls ($P<0.05$), but did not differ from the left hemisphere group ($P>0.05$). However, a significant left-right difference did appear when RAC was considered as a joint function of laterality of lesion and continuous observation. Right-hemisphere lesion resulted in a marked reduction in initial RAC, a generally lowered rate throughout the average 90-second OP, and an early increase to a reduced maximal rate.# Left-hemisphere lesions differed from the controls only in a depressed RAC during the final seconds of observation (Fig. 5).

Additional Observations.—Additional analyses which disregarded locus of lesion showed that neither post-traumatic epilepsy nor aphasia had any selective effects on reversal rate.

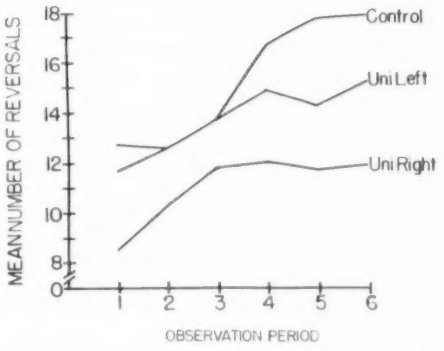

Fig. 5.—Rate of apparent change as a function of left and right hemisphere lesion×observation period.

The highly significant F-values for OPs and Conditions, when considered as main effects, were due to the pronounced tendency of all Ss, both normal and brain-injured, to report more reversals as continuous fixation proceeded, and during the second half of the testing procedure.

TABLE 5.—*Average Total Number of Reversals Reported by Subjects with Left and Right Hemisphere Lesions by Lobe Involved (Complementary Method of Classification)*

	Left	N	Right	N
Frontal	146.60	10	117.11	9
Parietal	181.18	11	141.75	8
Temporal	156.28	7	124.50	6
Occipital	144.75	4	63.50	2

Based on significant Group×OP interaction in the Left-Right analysis of Series (*a*); $P<0.05$.

Comment

There can be no doubt that perception of reversible figures was altered after brain injury. In this respect the present study confirms the work of others. However, contrary to conclusions of several previous investigators, such alterations did not arise solely from frontal injury. Lesion in any lobe of the brain was found to result in some change in figure reversal: either an increase or a decrease in total number of fluctuations seen, an altered time course of reversal rate with continuous or repeated observation, or a reduced RAC in the half of the visual field contralateral to the injured hemisphere. Which change or combination of changes occurred was found to depend on the locus of the lesion.

Effects of Unilateral and Bilateral Frontal Lesions.—The most striking finding was the contrast between RACs for unilateral and for bilateral frontal injuries. Unilateral frontal lesion resulted in marked lowering of reversal rates for the double cube, while bilateral frontal lesion caused a significant rise. Thus, bilateral frontal damage counteracted, so to speak, the deficit caused by unilateral lesion, or produced a change in the opposite direction. This effect is certainly difficult to relate to existing information on the effects of brain injury.

Many ablation experiments employing subhuman forms have shown that effects of unilateral damage, if at all manifested in behavior, were increased in severity and duration when the corresponding area in the opposite hemisphere was similarly destroyed. This outcome is so much expected in current animal experimentation that lesions are usually placed bilaterally without attempts at defining effects of unilateral ablation. Perhaps the present findings appear unique only because most experimenters fail to look for similar paradoxical effects. Systematic comparison of effects of unilateral and bilateral lesions in subhuman primates might reveal that the kind of result here obtained is not uncommon.

Our present results may give the impression that the opposite results of unilateral and bilateral lesions are unique for the frontal lobes. Such a conclusion may be correct, but our data are not sufficient to make it certain. Owing to the low survival rate of men with traumatic bilateral temporal lesion, there was no S with such a lesion in our group of patients. Few Ss with extensive bilateral occipital wounds could be included in the present sample because (*a*) survival is rare, due to proximity of vital brain stem structures, and (*b*) such lesions almost invariably produce homonymous field defects large enough to obscure the stimulus figures. Moreover, bilateral parietal wounds in this population tended to be parasagittal, grazing injuries, since missiles traversing both hemispheres more inferiorly would be likely to destroy vital diencephalic or mesencephalic centers. If our test figures should be presented to populations with extensive bilateral damage of nontraumatic (e. g., vascular) etiology, we might obtain the data necessary to assess the generality of our findings.

Notwithstanding these restrictions on the present data, the observed changes in figure reversal after frontal lesions were striking and demand interpretation. If an attempt is made to relate these present findings to other behavioral defects following frontal lesion in man, there is little convincing evidence that such injury does indeed result in specific changes.** Certainly, the classical "frontal-lobe syndrome," supposed to comprise deficiencies in ability for "abstraction" in its various forms and concomitant personality changes, has not been observed in the present subject population (Teuber, Battersby, and Bender[27]; Teuber and Weinstein[30]). Only two tasks other than tests of motor ability have so far

** Studies in many laboratories indicate that monkeys with frontal-lobe removals tend to fail delayed-response tests (Jacobsen[18]; Myer, Harlow, and Settlage[20]; Pribram, Mishkin, Rosvold, and Kaplan[21]). The reasons for such failure are still obscure, and as yet no comparable deficit in man following frontal injury has been reported.

uncovered special effects of frontal injury. Men with frontal lesions showed exaggerated constant errors in setting a luminous line to the objective vertical when their head and body were tilted (Teuber and Mishkin [29]). This effect has been attributed to an abnormal interaction between visual and postural stimuli. Similarly, tests of visual scanning in a complex field (Teuber, Battersby, and Bender [28]) have shown deficits in men with frontal lesions, with maximal prolongation of searching time occurring on the side of the field opposite the injury.

The apparent diversity of these effects raises the question whether frontal injury actually does result in derangement of some unitary function, or whether this aggregate of symptoms demonstrates the involvement of several discrete mechanisms which happen to share a common substrate. No a priori answer to this problem can be accepted, although any unitary interpretation has the advantage of parsimony. Should further study confirm that the divergent effects of unilateral and bilateral lesions on RAC are restricted to the frontal lobes, such unitary interpretation would have to encompass the present task involving response to reversible figures. Rather than attempt to offer such a unitary interpretation, we restrict ourselves to raising it as a question.

Effects of Right-Hemisphere Lesion.—Of special interest is the finding that men with right-hemisphere injury reported significantly fewer reversals than did men with left-hemisphere injury, since other findings point to the right hemisphere as being of particular importance in tasks which appear to require "spatial" judgments (McFie, Piercy, and Zangwill [16]; Teuber and Weinstein [30]; Ettlinger, Warrington, and Zangwill [8]; Weinstein, Semmes, Ghent, and Teuber [32]), and perhaps in those which involve simultaneous stimulation of both halves of the body (Critchley [6]). Milner [17] has published an excellent review of this material. A recent finding by Teuber [26] also indicates that right-hemisphere injury is significantly more predisposing to appearance of visual aurae in cases of posttraumatic epilepsy than is left-hemisphere lesion. Such results, as well as those of the present investigation, caution against all-too-simple concepts of hemisphere dominance. Apparently, some functions are more susceptible to injury of the right, and supposedly "nondominant," hemisphere. Unfortunately, it was impossible to obtain a sufficient number of left-handed Ss to analyze this question further.

Effects of Temporal Lesion.—The rather marked effect of temporal lesion on RAC found in the present study may be related to the role which has been attributed to temporal-lobe structures for the mediation of certain "visual processes." Since the demonstration of Klüver and Bucy [14] that bilateral temporal lobectomy produces profound behavioral alterations in the monkey, other investigators (Chow [4]; Riopelle, Alper, Strong, and Ades [25]; Mishkin and Pribram [18]) have repeatedly shown that lesions restricted to the ventromedial temporal cortex impair visual discrimination performance in a nearly selective manner. This deficit cannot be attributed to a more general memory defect as such, for such animals can successfully learn tactile discriminations. Neither is the deficit due to any gross impairment of visual acuity or the presence of a field defect in peripheral vision; animals with extensive field defects following occipital lesion have no comparable difficulty with visual discriminations. Milner,[17] in the review cited earlier, concludes that, in the monkey, bilateral temporal lesion produces deficits in visual learning and retention; in man, even unilateral temporal damage causes difficulty in understanding "complex pictorial material." One cannot help wondering whether such difficulties as Milner describes are, like our changes in RAC, more apparent in the half-field contralateral to the lesion and most pronounced after prolonged exposure to the task. However, it must be noted that changes in RAC in our study were not

unique for Ss with temporal-lobe involvement.

Nature of the Changes.—How can the alterations in perception of figure reversal be characterized? First, we conclude that reversal rate is determined by several mechanisms acting conjointly but not completely sharing the same substrate. Second, as regards the level of function which such mechanisms represent, reversal rate is not determined wholly by first-order events at the striate cortex, as shown by the vulnerability of RAC to lesions far removed from the optic pathways and not accompanied by scotomata. This view is strengthened by the fact that, in normal Ss, reversal rate for a single cube is increased only by prior inspection of figures with phenomenal similarity of form and is unaffected by prior inspection of figures whose contours are merely in close retinal proximity to, or even coincident with, the cube contours (Cohen [5]). Other features of RAC after brain injury, such as lack of significant correlation with general intelligence or presence of aphasia, and occurrence of significant differences between the halves of the visual field in some subgroups, argue against the possibility that the observed deficits are of a very general nature, e. g., impaired intellectual function, language disability, and the like. Rather, these processes probably lie at some intermediate level of complexity, comparable (in this sense at least) to difficulties which have classically been termed agnosia. The nature of such processes is, as yet, utterly obscure; and, indeed, the possibility that such mechanisms can ever be conceptualized in psychological terms, rather than in terms of fundamental physiological processes, is, of course, impossible to assess. Nevertheless, a more complete understanding of the effects of brain injury on figure reversal, and other deficits as well, depends on the specification of the nature of such mediating events.

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A Combined Test Used for the Diagnosis of Organic Brain Condition

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The psychological examination of the brain-injured patient is now being introduced more and more routinely as an integral part of the general diagnostic procedure in neuropsychiatric clinics.[1,3,18] The usual testing tools applied are visual designs tests (Bender,[4,9,15,26] Ellis,[11] Benton [6,8]), the tests designed by Goldstein and his coworkers,[12] Wechsler's Intelligence Scale,[17, 25,31] the Marble Board test,[30] Rorschach's technique,[2,16,19,20-22,27] and Goodenough's Draw-a-Man test.[5,7,13]

Important and helpful as all those tests are, they do not easily lend themselves to quantification. The present paper presents a combined test, relatively short (administration and scoring takes about 10 minutes), which lends itself to objective scoring and to qualitative analysis as well.*

The plan of presentation is as follows: (1) First, the test will be described; (2) a validating study will be reported, and (3) the qualitative aspects of the test and the interpretation of positive test findings are discussed.

I. The Test

Administration.—The test is composed of the following three parts:

1. Drawings: This section consists of four cards, illustrated in Figure 1. The subject is presented with Card 1 and is told that he will be asked to reproduce the design after he has finished looking at it. This time varies from subject to subject but is not limited by the examiner. When the subject has completed the first design, he is presented with Card 2, and this procedure is repeated with the remaining cards.

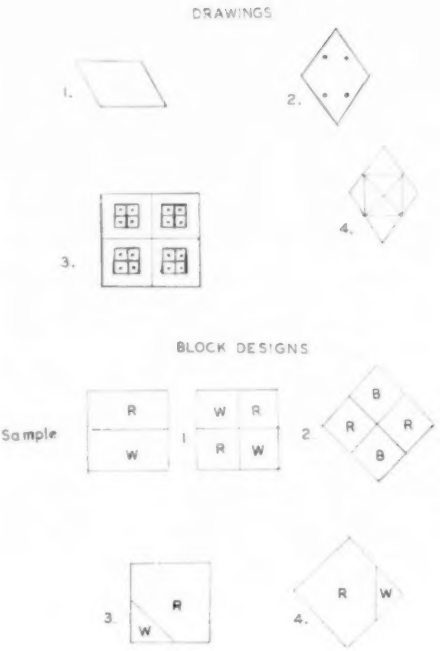

Fig. 1.—Drawings and Block designs. Reduced to one-fourth size.

2. Blocks: The subject is required to arrange four blocks (the usual Kohs blocks) according to a design placed before him. He is given a demonstration by the examiner with the sample card illustrated in Figure 1. The design remains before the subject until he has completed it and is ready for the next one. The examiner notes whether the subject has succeeded and how much time was needed. In case of failure, the examiner records the design made by

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* The present work is the result of eight years of cooperative work with approximately 15 neurologists and psychiatrists in the neuropsychiatric clinic of Kupat-Holim Zamenhoff.

the subject, since this serves as a basis for the scoring. The sample and the four designs are reproduced in Figure 1.

3. Digits: The examiner reads aloud 20 series of 5 digits each at the rate of one digit per second and asks the subject to repeat them. The examiner notes whether the subject has succeeded or not, and, again, in case of failure he jots down the exact digits said by the subject.

Scoring.—Although the test items themselves have been taken from well-known scales, the scoring system used here has certain significant changes. The guiding principles in developing the present scoring system were as follows:

1. Instead of the usual procedure of scoring either success or failure, it was decided to score the *degree of failure.*

2. Only such mistakes have been scored as have been found to be typical of brain-damaged people.

The special instructions for scoring each subtest are in brief as follows:

1. Drawings

	Points
(*a*) Misdirection of any line	1
(*b*) Addition or omission of a line	2
(*c*) Misplacement of any dot	½
(*d*) Addition or omission of a dot	1
(*e*) Repeated failures in all four little squares of Figure 3 are scored only once, while repeated failures in all 16 tiny squares of that drawing are scored twice.	

2. Blocks

	Points
(*a*) Any block located in the right place and on its right side but in the wrong direction	1
(*b*) Any block located in the wrong place	2
(*c*) Any block placed on a wrong side	2
(*d*) The whole design misdirected	2
(*e*) Time. Points are added according to the following	

	Points
16-19 min.	1
20-29 min.	2
30-39 min.	3
40-49 min.	4
50-	5

3. Digits

	Points
(*a*) Displacement of any digit	1
(*b*) Substitution of any digit	2
(*c*) Addition or omission of any digit	2

The results are summarized in two halves, containing 10 series each.

II. The Experiment

Subjects.—The present experiment compares the test results achieved by two groups, an "organic" and a "nonorganic," containing 35 subjects each.

The organic group consisted mostly of patients of the neuropsychiatric clinic of Kupat-Holim Zamenhoff, partly of patients hospitalized in the neurological and neurosurgical departments of Beilinson Hospital, Petach-Tikva. All cases were definitely diagnosed by experienced neurologists as "organic" and belonged to a variety of syndromes: epilepsy; encephalitic state; brain hemorrhage; state after brain operation; meningitic state; arachnoiditis, intracranial, and migraine.

The nonorganic group was composed of a random selection of school children and adults who had never been referred to a neurologist or psychiatrist, nor had suffered from paroxysmal headaches or had shown any tendency to faint.

Both groups were reasonably matched for the categories of sex, age, and intelligence, as is shown in Table 1.

Main Results.—The main results are indicated in Table 2. The results evidently support the hypothesis that the test differentiates the organic from the nonorganic group at the statistically significant level.

TABLE 1.—*Distribution of Sex, Age, and IQ of the Organic and Nonorganic Groups*

	Sex		Age		IQ	
	Male	Female	Mean	σ	Mean	σ
Organic (N=35)	22	13	21	12	98	11
Nonorganic (N=35)	21	14	20	12	99	9

TABLE 2.—*Comparison of Scores of the Organic and Nonorganic Group*

	Drawings		Blocks		Digits	
	Mean	σ	Mean	σ	Mean	σ
Organic (N=35)	15.8	8.8	6.0	5.0	15.9/20.8	9.3/12.8
Nonorganic (N=35)	6.2	5.9	3.0	3.0	6.5/7.8	5.6/5.7
Mean difference is significant at the level of	0.01		0.01		0.01	

TABLE 3.—*Organic Norms for the Three Subtests*

	Points
Drawings	10
Blocks	5
Digits	10/10 or 0/15

TABLE 4.—*Organic Findings in the Organic and Nonorganic Groups*

Organic Findings	Organic Group N=35	Nonorganic Group N=35
In all 3 subtests	7	0
In 2 subtests	23	6
In 1 subtest	4	9
No organic finding	1	20
Total	35	35

The question now arises whether the present test is as efficient a tool for diagnosis of individuals as it is for groups. To answer this question, it was necessary to define the meaning of "Organic Finding" for each part of the test. Table 3 indicates the organic norms for the three subtests, so that a subject who has attained a score on any subtest at least as high as is indicated in the table is said to have an "Organic Finding" on that subtest.

Table 4 summarizes the organic findings obtained in both groups. Now, if we assume that a subject who shows organic findings at least on two subtests is to be considered to have an organic disease, the test has correctly diagnosed 30 out of 35 organic cases (86%).

Similarly, if a subject who fails on no more than one subtest is considered not to have an organic illness, then the test has correctly diagnosed 29 out of 35 nonorganic cases in the sample (83%).

Table 4 also makes clear why it was necessary to combine three parts in a test of organicity. A test based on one item only, however elaborated it may be, inevitably misses the diagnosis of some organic cases, while it may wrongly diagnose some nonorganic cases as organic.

III. Comment

Analysis of the typical failures of the organic patients in the test yields valuable conclusions in two directions: first as to the general psychological rationale of the functions required by the three parts of the test, and, second, as to the description of some basic mental deficiencies of the organic patient. This section will be devoted first to a discussion of the qualitative aspect of the test, then to the interpretation of positive test findings.

Qualitative Analysis

Drawing and Digits Subtests.—These tests, in the way they are administered here, show some basic features in common which make it possible to treat them together. We shall first take them up and then proceed with the discussion of the Blocks subtest.

In the Drawings, as well as in the Digits, the subject is confronted with a series of stimuli (visual and auditory), is asked to retain them properly, and then to reproduce them correctly (to draw or to verbalize). Both tests are therefore *perceptive-retentive-motor* tests, as viewed from the mental faculties involved. The qualitative analysis offered here, however, is based on the perceptive-retentive qualities only, although I am well aware that useful clues may be drawn from the motor quality of the test as well (e. g., trembling in the drawing, speech difficulties, and peculiarities in the reproduction of the digits).

Success Factors: It is assumed that success in the Drawings and Digits depends on the following:

1. Proper perception. The subject has, first of all, to "take in" precisely and fully the visual (Drawings) and auditory (Digits) stimuli.

2. Proper retention. Unless the subject retains the impressions properly, he is unable to reproduce them.

3. Proper "localization." Not only do the "imprints" have to be retained somewhere and somehow in the central nervous system, but they ought to be preserved there in the right spatial (Drawings) and temporal (Digits) order.

Failures: A defect in the ability of *perceiving* and/or that of *retaining* properly will produce the following three types of failures:

1. Omission. A part of the drawing or the digits is omitted from the subject's reproduction. The omission is often accompanied by a subjective feeling that induces the subject to apologize for not having paid enough attention (failure in perception) or for having already forgotten a part (failure in retention).

2. Confabulation. The subject fills in the "void space" by inserting items from his memory aroused in his mind by way of association. In this case, as well as in perseveration (3), the subject mostly has no idea of doing wrongly.

3. Perseveration. Previous test impressions continue to influence the subject's mind and help to falsify the reproduction of the new ones.

Defect in the faculty of *localization* will yield the following type of failure:

4. Disorientation. The subject's reproduction contains all the original details but in the wrong order. This type of failure reflects the well-known difficulty of the organic patient to orient himself properly in space, as well as in time.

Examples of failures in the Drawings are given in Figure 2. Examples of failures on the Digits subtest are as follows:

Omission: 4275 instead of 42785. Sometimes more than one digit is omitted, and occasionally one meets a subject who is unable to repeat even a single digit of a series. One such patient explained spontaneously: "It was as if I had fallen asleep for a while." Such a phenomenon reminds one strongly of a temporary loss of consciousness met with in petit mal.

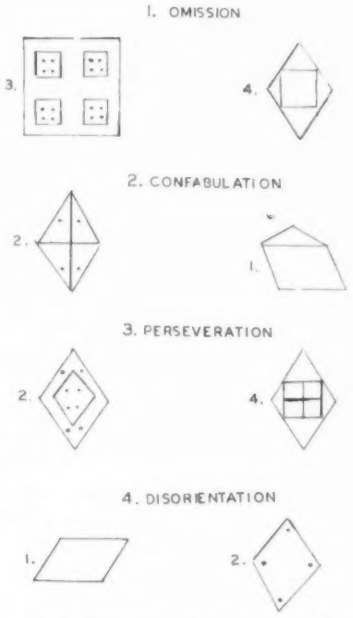

Fig. 2.—Various types of failures in the Drawings.

Confabulation: 823479 instead of 82479.

Perseveration: 72669 instead of 72649.

Disorientation: 37958, or even 38579, instead of 39758.

5. Compensation. Careful observation of the subject's performance may yield a further characteristic of the organic patient which is not reflected in the scoring. This characteristic may be called compensation. The subject compensates for his deficient visual or auditory "centers" by making use of other, better-preserved abilities. Thus, a man, of 67, who failed badly in the reproduction of the third drawing succeeded satisfactorily on the last one after having "translated" the visual stimuli into verbal ones. While he was watching the figure, he murmured to himself: "Diamond, enclosed square divided by two diagonals."

Similarly, one often encounters subjects who carry out writing movements in the

air while listening to the digits, or who repeat to themselves each digit silently after the examiner.

The *Digits* subtest allows for two more types of failures, which have been noticed typically in the organic patient.

6. Sensitivity to noise. The slightest noise coming from outside may at times throw the subject entirely out of his concentration, so that he cannot repeat any digit of the last series, leaving the examiner in doubt whether or not to score the failure as such. Anyhow, this fact in itself is worth being noted by the examiner, since in a number of cases it proved to be a good indication of organicity.

7. Fatigue. It is a well-known fact that the organic patient is liable to show early signs of fatigue, especially if he is induced to sustained effort in an area in which he is deficient. This characteristic may show up on the digits subtest in two ways.

(*a*) Quantitatively. The errors in the later series are significantly more than those in the former. The test contains 20 series to make possible the comparison between the total score of the first 10 series with that of the last 10. In this respect there seems to be a difference between the nonorganic and the organic subject. The nonorganic subject shows very often an improvement in the latter half of the test, probably because he has become accustomed to the new task, or because he may have hit upon an expedient method of doing it. Contrariwise, the organic patient is more liable to show signs of progressive decline in performance, probably because of fatigue.

(*b*) Qualitatively. The subject reveals signs of tiredness in his behavior or verbalization. He may stretch out his arms, move in his chair, touch his face, yawn, etc. Or he may express himself grudgingly that he has enough of it; he may become critical of "that kind of test," and at times he may complain of being attacked suddenly by a headache. One patient said that he felt as if he was going to faint.

Blocks Subtest.—The subject's function is to arrange four blocks according to a visual guide, which remains all the time before him. Thus in this case no power of retention is called for, and the test may be regarded, in accordance with Rapaport's [28] point of view, as one of visual motor coordination.

Originally, Kohs designed this test as a measure of intelligence, for he assumed that the test calls for analytic and synthetic abilities. Wechsler,[31] who included this test in his Intelligence Scale, regarded it as "the best single performance item," which also correlates highly (r=0.73) with the total score of his scale.

Since our intention, however, was to test for brain damage rather than to measure intelligence, it was necessary to include in the present test only very simple designs, such as would not require a mental age of more than six or seven years for their proper performance. Our experience with the Block test is in accord with that of Wechsler,[31] who stated that "most cases of brain disease often cannot complete the simplest design, however much they try."

As to the rationale of this test, it is assumed that the subject's main task lies in grasping correctly a visual *Gestalt*, so as to be able to reproduce it through proper manipulation of the blocks. In order to succeed, the subject must be guided simultaneously by three aspects: *color*, *form*, and *localization*. Therefore, failures may be classified according to the same three aspects.

1. Disregard of *color*. The subject places the four blocks together so that they reproduce the square form of the design and shows no concern whatsoever in matching the design's colors.

2. Disregard of *form*. This may happen in two ways:

(*a*) Disregard of the square form of the design.

(*b*) Disregard of the pattern of the colors, although using the correct colors in themselves.

3. Disregard of *localization* (disorientation). This, too, may be of two types:

(*a*) The relative position of the colors in the design is changed.

(*b*) The whole construction is placed at a wrong angle on the table.

An additional type of failure:

4. Slowness. This may be the result of the following:

(*a*) After the subject has completed his construction, he realizes that it does not match the design because of his not having paid attention to all of its aspects. He then renews his efforts until he succeeds, thereby lengthening the time of his performance.

(*b*) The subject shows definite lack of dexterity in the way he manipulates the blocks. One could often detect a tendency to perseveration, which disturbs the smooth performance. Goldstein [12] has already called attention to the way in which some organic patients handle the blocks: They turn them all the time in one direction only and thereby fail to notice two sides of them. The well-known difficulty of the organic patient in "shifting" may also be regarded as a special form of motor perseveration.

The various failure types in the Blocks test are reproduced in Figure 3.

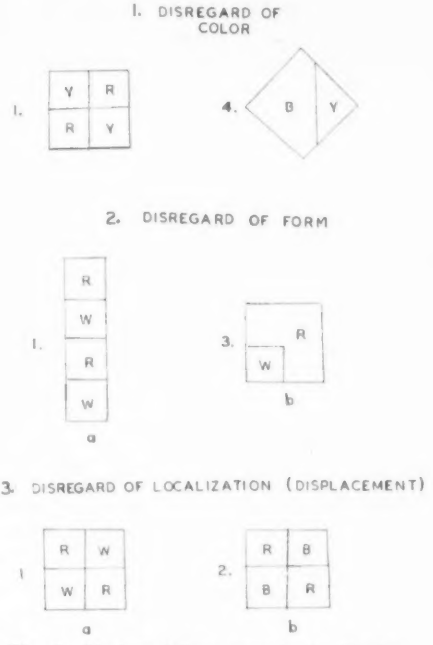

Fig. 3.—Various failure types in the Blocks.

Interpretation of Positive Test Findings

Perhaps the most important aspect of the test, namely, its meaning, will now be discussed. The question may be formulated simply: *A*. What do positive test findings *mean*? *B*. Which clinical symptoms might possibly accompany such findings?

A. At the present stage of the study it is only permissible to make the general statement that positive test findings reflect some *defective or deficient brain condition*. No specific diagnosis as to the type of organic damage or its "localization" can as yet be made with any certainty. Of course, this does not exclude the possibility that a clinician, after having enough experience with the test, might formulate some hypotheses as to the more specific diagnosis of a given case. Such hypotheses should always be further tested by an extensive neurological examination.

The organic brain condition hinted at by the test may be of the following varieties:

1. Congenital defect or deficiency of the brain.

2. Defect in the brain as a result of some disease or trauma. The meaning of "brain defect" is naturally not confined to the brain tissue alone but might include as well defects in the vessels, hormones, or other parts of the organism which affect directly or indirectly the proper functioning of the brain.

3. Defect or deficiency of the brain such as appears "normally" with old age.[31] Theoretically this might be considered as a special subtype of the former category.

It should be clearly stressed that none of the above-mentioned brain conditions is necessarily always accompanied by positive neurological findings. This test is, therefore, like other psychological tests of organicity, frequently more sensitive as a diagnostic tool than is the usual neurologi-

cal examination. This "sensitivity" has been revealed in two ways.

1. Most of the patients in whom the neurologist has found organic involvement produced organic findings in the psychological test as well.

2. Contrariwise, there appeared a good number of cases with psychological positive findings in which no essential neurological verification was produced.

It should, however, be pointed out that in *some* of the last-mentioned cases neurological symptoms appeared later on. Such cases give evidence to support the *predictive* value of the psychological test. Our experience in this respect coincides with that of Wechsler,[31] who stressed "the value of Scale in detecting possible organic brain conditions prior to manifestation of neurological symptoms." Wechsler illustrated this by "a striking case of a 19 year old boy who was admitted to the hospital after an attack of dizziness and transient loss of memory."

A neurological examination on admission was essentially negative. He improved very quickly and was discharged after a short period of observation with a tentative diagnosis largely based on the patient's attitude towards his illness, of conversion hysteria. During this first stay, a psychometric examination (Wechsler-Bellevue) revealed a number of "soft signs" which led the psychologist to suggest the possibility of organic involvement. As there was no medical substantiation at the time of an organic brain disease, no special regard was paid the psychologist's observation. Three months later the patient was readmitted to hospital with a full blown brain tumor.

B. As to the question, which *symptoms* might be expected to accompany positive test findings, one has to consider the following possibilities:

1. "Somatic" symptoms, such as epileptic seizures, fainting spells, migraine headaches, and tics.

2. "Mental" symptoms, such as loss of memory, difficulty in concentration, excitability, restlessness, aphasia, and other speech difficulties.

3. Psychopathic behavior. A number of psychopaths, as well as children with severe behavior disorders, have been found to yield organic findings in the test. This, rather, should raise little wonder, since electroencephalographic studies have recently revealed cerebral dysrhythmia in a considerable percentage of psychopaths.[10, 23, 29] Thus, the well-known inability of the psychopath to control his impulses (in psychoanalytic language, his deficient superego), as well as his inability to gain by experience (in a sense, learning difficulty) might be founded, at least in certain cases, on an organically deficient brain.

4. Special school difficulties, as in reading and arithmetic. The test supports other clinical findings that reading and arithmetic difficulties can frequently be traced to organic damage.

5. Absence of overt symptoms but strong evidence of a defective or deficient inherited "organic" constitution. Although I have not designed any special experiment on "organic" heredity, I was struck at times by the fact that positive organic test findings were found in close relatives (children or parents) of patients suffering from epilepsy or migraine.

It should be noted that similar results have been found in electroencephalographic studies of relatives of epileptics.[11, 23, 24]

Evidently, much experimental work is still needed in each of the directions outlined above. It is my belief that the present test will be useful as a convenient research tool, for the following reasons: It is easy to use; the time required for administration plus scoring is in most cases less than 10 minutes, and the scoring system is simple and unequivocal.

From the above discussion, it becomes clear that people with organic damage do not always produce positive findings in the neurological examination as it is practiced today. This fact should be taken into consideration in any further experimental research which undertakes to compare organic and nonorganic groups on the basis of the present test. The "nonorganics" should exclude not only patients with overt neurological symptoms but also people showing any of the above-listed symptoms, as well

as those who are heavily loaded in their heredity.

Summary

A test purposing the diagnosis of organic involvement is described. The test consists of three parts: Drawings, Blocks, and Digits. A special scoring system is elaborated for each part of the test which enables the examiner to assign a number of points to each of the subject's responses.

Test scores of a group of 35 organic patients were compared with those of a similar group of nonorganic subjects. Score differences were found to be significant. An assumption was made that subjects showing "organic findings" (scores beyond a defined minimum) at least on two parts (any parts) of the test are to be considered "organic," whereas all others are regarded as "nonorganic." Accordingly, 86% of the organic cases and 83% of the nonorganic cases were diagnosed correctly by the test.

The following rationale has been proposed for the three parts of the test. Success in Drawings and Digits depends mainly on proper functioning of perception, retention, and localization. Success in Blocks depends largely on the subject's ability to be guided simultaneously by color, form, and the localization of the design. Failures were analyzed and assorted in accordance with the proposed rationale, quantitatively as well as qualitatively; and conclusions were drawn regarding some basic mental deficiencies of the organic patient.

Positive test results generally reflect an "organic brain condition" of the following types: (1) congenital; (2) as a result of trauma or disease; (3) as a result of senescence.

Subjects with positive test results may show (1) somatic symptoms, (2) mental symptoms, (3) psychopathic behavior, and (4) special school difficulties (children) or (5) they may have close relatives suffering from a brain disease (epilepsy, migraine, etc.).

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Drug Therapy, Milieu Change, and Release from a Mental Hospital

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Introduction

The concept "therapeutic milieu" implies that the relations of mental hospital patients to each other and to the hospital staff can be structured to encourage recovery. In contrast to milieu as therapy, the tranquilizing drugs employ physiological means to effect action within individual patients. However, milieu effects may be interwoven with drug effects.*

This study was designed to answer questions about milieu changes concurrent with the use of the tranquilizing drugs chlorpromazine and reserpine. The questions were as follows:

1. Are patients treated with chlorpromazine or reserpine in their first admission to a mental hospital more likely to be released to the community during the first year of hospitalization than a comparable group of patients hospitalized before the use of drugs?

2. Are patients *not treated* with chlorpromazine or reserpine but hospitalized for the first time during the recent period of drug therapies more likely to be released to the community than a comparable group of patients hospitalized before the use of drugs?

3. Are patients hospitalized for the first time during the recent period of drug therapies less or more likely to return to the hospital within a year after release than are similar patients hospitalized before the use of drugs?

In answer to Question 1, it was anticipated that the data would confirm many reports about the therapeautic effectiveness of chlorpromazine and reserpine. Question 2 sought an answer about milieu change in the wake of extensive use of the drugs. The assumption was that institutional change could best be isolated from direct drug effect by studying patients *not* treated with the drugs but hospitalized during the period of widespread drug use. Question 3 asked whether patients' recovery conjoined to drug therapy or milieu change was likely to be sustained for at least one year after release.

To answer each question, a before-after experimental design was simulated. This was done by using the release and return rates of the period prior to the use of drugs as a base from which to measure changes in release and return rates of the period of drug therapies.

Study Data and Sample

Source of Data.—St. Elizabeths Hospital, the Federal hospital for the District of Columbia, allowed me access to the medical records of patients admitted during the years 1953 through 1956. Information was abstracted from (1) psychiatric interviews with the patient and with informants who know the patient, (2) social service interviews, (3) medication orders, (4) nursing notes, and (5) orders for seclusion and restraint.

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Eleanor E. Carroll made a critical review of this paper.

*It is difficult to anticipate therapeutic effects of the milieu or to detach such effects, if anticipated, from drug effects. Minimum controls may be achieved by a double-blind procedure, in which neither patients nor clinical staff knows which patients are given a placebo and which are given the drug. Nevertheless, this does not eliminate the effects of social meanings of medications or of improvements in social environment concomitant with the use of drugs.

Subjects Selected for Study.—Patients meeting the following criteria were selected for study:

1. Diagnoses: Functional Psychoses only (schizophrenia, manic-depressive psychoses, involutional psychosis)
2. Age: Range 20 through 49
3. Race and sex: White persons and Negroes, both sexes
4. Residence: Residence in the District of Columbia for one year or more
5. Date of admission: Admission to the hospital during the period Jan. 1, 1953, through Aug. 31, 1956, and no prior hospitalization in a mental institution extending beyond one month

The following types of patients were excluded even if they met the above criteria:

1. United States prisoners
2. Patients transferred to another hospital or discharged without medical approval within the first year of hospitalization
3. Those who died within the first year of hospitalization

For the period of investigation, 582 of the just over 5,000 admissions to the hospitals were included in this study. Nearly all the patients were diagnosed as schizophrenic—just under 90%. Five per cent had involutional, and 4% manic-depressive psychosis. The median age of the group was in the early 30's. Thirteen per cent of the selected patients were white men; 29%, white women; 20%, Negro men; and 38%, Negro women.

Time Interval Studied.—Patients were followed from admission to release or to the end of the first year after admission, whichever came first. "Release" was the first time the patient went into the community for a trial period of living away from the hospital. Some patients were discharged directly from the hospital without having had such a trial visit; in these cases release coincided with discharge.

If a patient was released during the first year, his record was checked to determine whether or not he had returned to the hospital within one year after release.

Drug Treatment and Probability of Release

Patients admitted for the first time during 1955 or 1956 had a greater chance for release within one year of admission than those admitted for the first time during 1953 or 1954† (Table 1).

Treatment with chlorpromazine and reserpine was begun in the middle of 1954, but such treatment did not increase the chance for release of patients admitted in that year. In fact, among patients admitted during 1954, those treated with drugs were *less* likely to be released than those not so treated.

Lack of firm standards of dosage and length of treatment could not entirely account for the fact that the release rate of 1954 admissions treated with drugs was lower than that of 1955-1956 admissions. Notwithstanding when treatment was begun, low or high maximum dosages, and relatively short or long treatment, the release rate of 1955-1956 patients for each subgroup was greater than the release rate of 1954 patients.

† Unless noted to be statistically not significant, all differences, if discussed, are statistically significant. The standard for significance was that the difference would have arisen by chance only in 5% or less of the samples drawn from the universe.

TABLE 1.—*Per Cent Released Among Patients Treated or Not Treated with Chlorpromazine or Reserpine, by Year of Admission*

Year of Admission	Per Cent Released Among Treated	Number Treated	Per Cent Released Among Not Treated	Number Not Treated	Total Per Cent Released	Total Number Admitted
1953	*	2	43%	162	43%	164
1954	23%	65	45%	109	37%	174
1955	65%	104	71%	38	67%	142
1956	69%	93	*	9	71%	102

* Per cent not shown because base is less than 10.

Among 1955-1956 admissions, the difference in release rates between treated and nontreated patients still favored the nontreated, but the difference was small and not statistically significant.

Drug Treatment for Hyperactivity and Probability of Release

Selection of Patients for Drug Treatment.—Among 1953 admissions in the study, only two patients were treated with chlorpromazine or reserpine before their first release or during the first year of hospitalization. Of the 1954 admissions, 37% were treated; of the 1955 admissions, 74%, and of patients admitted between Jan. 1 and Aug. 31, 1956 (the cut-off admission date for this research), 92%.

In its initial use of the drugs, St. Elizabeths, in agreement with repeated clinical findings concerning the type of patients with whom the drugs proved most efficacious, tended to select hyperactive patients for treatment:

> As a rule, patients were selected, not by their psychiatric diagnosis, but on the symptomatic criteria that they were agitated, destructive, assaultive, noisy, combative, and overactive.‡

By 1955-1956, however, the reason for recommending drug treatment was often the anticipation of hyperactivity or the persistence of abnormal mental symptoms.

In this study, a patient was classified as hyperactive if the nursing notes described him at *any time* prior to first release or the end of the first year of hospitalization by *any one* of the following terms: anxious, destructive, assaultive, threatening, given to shouting or running about. Any behavior described as provoked was not considered hyperactive behavior.

Drug Treatment of Hyperactive Patients and Probability of Release.—There was little or no change between 1953 and 1954 in the proportion of hyperactive patients who were released within the first year of hospitalization. However, a considerably larger proportion of hyperactive 1955-1956 patients were released (Table 2).

The physiological effects of the drugs alone cannot account for the higher release rate of hyperactive 1955-1956 patients. Such patients, whether or *not* they were treated with drugs, were much more likely to be released than were hyperactive 1953-1954 patients. Also, treatment of hyperactive 1954 patients with drugs did not enhance their chance for release.

Treatment of Nonhyperactive Patients and Probability of Release.—Results similar to those described above for hyperactive patients were obtained for patients not classified as hyperactive. In short, nonhyperactive 1955-1956 patients, whether or not they were treated with drugs, were more likely to be released than were nonhyperactive 1953-1954 patients.

Reliability of the Classification for Hyperactivity.—It is possible to question the reliability of the use of nursing notes as a source of classification for hyperactivity. Some nurses and attendants may tend to

‡ A statement similar to that by Waldrop[1] was made about the selection of patients for treatment with chlorpromazine at St. Elizabeths.[2]

TABLE 2.—*Per Cent Released Among Hyperactive Patients Treated or Not Treated with Chlorpromazine or Reserpine, by Year of Admission*

Year of Admission	Hyperactive Patients				Total Per Cent Released	Total Number Admitted
	Per Cent Released Among Treated	Number Treated	Per Cent Released Among Not Treated	Number Not Treated		
1953	*	2	36%	101	35%	103
1954	24%	59	39%	54	31%	113
1955-1956	63%	116	69%	13	64%	129

* Per cent not shown because base is less than 10.

TABLE 3.—*Per Cent Released Among Nonhyperactive Patients Treated or Not Treated with Chlorpromazine or Reserpine, by Year of Admission*

	Nonhyperactive Patients					
Year of Admission	Per Cent Released Among Treated	Number Treated	Per Cent Released Among Not Treated	Number Not Treated	Total Per Cent Released	Total Number Admitted
1953			56%	61	56%	61
1954	*	6	51%	55	48%	61
1955-1956	73%	81	76%	34	74%	115

* Per cent not shown because base is less than 10.

enter notes perfunctorily, considering such duties relatively unimportant. The notes may become increasingly sporadic the longer the patient is in the hospital. Most important, perhaps, nurses and attendants may either not be present when hyperactive behavior occurs or fail to be aware of it.

However, the classification of a patient was based on *any* hyperactivity ascribed to him prior to first release or by the end of the first year of hospitalization. It is highly improbable that every instance of hyperactivity would be unrecorded by the nursing staff. Furthermore, hyperactivity is very likely to be recorded because it is an obvious kind of behavior. Finally, the hospital is responsible for the physical well-being of patients, and, at the very least, any assaults or threatened assaults would have to be recorded.

In any event, the logic of the argument in this paper is based on comparisons. There is no reason to believe that any omissions would be more likely to occur for one of the several types of patients compared than for the others.

However, establishing with some certainty that the improved chance for release was shared by nonhyperactive patients as well as hyperactive patients is necessary to the discussion below of plausible explanations for the higher release rate among 1955-1956 admissions. Consequently, a second measure of hyperactivity was employed, the seclusion orders. Seclusion selects out patients who were more hyperactive than do the nursing notes, since it is usually reserved for continuing and threatening types of hyperactivity. If seclusion orders are used to classify patients as hyperactive, the findings of Tables 2 and 3 are confirmed.

Release Rates

There are several factors, other than drug treatment, which may affect the probability that a patient would be released from a mental hospital. They include such things as the following:

1. *Social History Prior to Hospitalization.*—It is conceivable that fluctuations in release rates from year to year could be a function of differences in patients' prehospital social histories. Data were collected about many such factors—occupational history, religion, church attendance, marital status, how long married, drinking habits, etc. None of these were associated with the increase in release rates for 1955-1956 admissions.

2. *Diagnosis and Symptoms.*—There were scarcely any changes between 1953 and 1956 in the proportion of patients falling into each of the several diagnostic categories that comprise the functional psychoses, or in the proportion of patients who showed certain types of symptoms prior to hospitalization.

3. *Hospital Admission Policies.*—Nearly all patients (94%) studied came from the psychiatric department of the city hospital. All such cases are committed after a hearing before a Commission on Mental Health, and St. Elizabeths must accept them. During 1953 through 1956 there were no changes in procedures for commitment or

TABLE 4.—*Per Cent Released Within Race-Sex Groups, by Year of Admission*

	Whites						Negroes					
Year of Admission	Per Cent Males Released	Number of Males	Per Cent Females Released	Number of Females	Per Cent Whites Released	Number of Whites	Per Cent Males Released	Number of Males	Per Cent Females Released	Number of Females	Per Cent Negroes Released	Number of Negroes
1953	43%	23	56%	54	52%	77	22%	27	40%	60	34%	87
1954	36%	25	53%	43	47%	68	29%	38	31%	67	30%	105
1955	57%	14	67%	45	64%	59	67%	24	70%	59	69%	83
1956	69%	13	85%	26	79%	39	60%	25	70%	37	66%	62
Difference between 1955-1956 & 1953-1954	23%		19%		21%		37%		34%		35%	

admission. Moreover, the number of *total* admissions by year scarcely changed in this time, and, consequently, there was no increase in pressure for space to house patients.

4. *The Patient's Experience in the Hospital.*—Up to this point drug treatment has been considered as perhaps the major factor in the hospital setting relevant to release. However, other experiences of the patient in the hospital may be associated with changes in release rates.

(*a*) Treatments Other than Drugs: The major treatments, other than drugs, in use during the period of study were insulin coma and electroshock. Thirty-five per cent of the patients admitted in 1953-1954 were treated with either of these methods. The drugs tended practically to eliminate the use of these therapies with 1955-1956 patients: Just 7% of the 1955-1956 patients were so treated. However, these treatments did not have any relevance to the difference in release rates between 1953-1954 admissions and 1955-1956 admissions. Treatment with either therapy did not increase to a significantly statistical extent the probability of release, regardless of the year of admission.

(*b*) Desegregation: Prior to 1955, patients, at admission, were assigned to different services on the basis of race and sex. Racial desegregation on admission services began in the latter part of 1954.

It was not known, in advance, in what ways desegregation might affect Negroes or whites. The fact is that release rates increased markedly between 1954 and 1955 for both Negroes and whites (Table 4). If desegregation were the major cause of improvement in the mental conditions of patients, it is surprising that it should have made its influence felt so immediately and so sharply for members of both races, since some tensions might have been anticipated during the first year. (Both the Negro and the white patients tend to be originally from southern states.) In short, desegregation may have contributed to the improved release rates. It does not seem plausible, however, that this fact alone could explain the extent of the improvement that occurred for both Negroes and whites.

(*c*) The Quieter Atmosphere of the Hospital: It might be posited that chlorpromazine and reserpine, in reducing hyperactivity among treated patients, induced a quieter, less provocative environment from which *all* patients benefited.§

Of patients admitted in 1955-1956 and hyperactive during their first three months in the hospital, 65% became nonhyperactive during the remainder of their first year of hospitalization or up to first release.‖ This was a considerably greater change than occurred among 1953-1954 admissions (Table 5). Furthermore, patients admitted in 1955-1956 who were not hyperactive in the initial

§ Reduced hyperactivity of nontreated patients as a consequence of reduced hyperactivity of treated patients has been noted in other studies (Wing[3]; Levin[4]).

‖ If number of months of hospitalization is held constant, the pattern, by year of admission shown in Table 5, is repeated.

TABLE 5.—*Patients Hyperactive and Nonhyperactive First Three Month: Who Became or Remained Nonhyperactive, by Year of Admission*

Year of Admission	Per Cent Hyperactive First 3 Mo. Who Became Nonhyperactive 3.0-11.9 Mo., or to Release	Number Hyperactive First 3 Mo.	Per Cent Nonhyperactive First 3 Mo. Who Remained Nonhyperactive 3.0-11.9 Mo., or to Release	Number Nonhyperactive First 3 Mo.
1953	41%	90	82%	74
1954	38%	91	73%	83
1955-1956	65%	115	89%	129

three months of hospitalization were more likely to remain nonhyperactive¶ (Table 5).

The change in the atmosphere of the hospital induced by decreased hyperactivity may be of considerable importance in explaining the improvement in release rates. This will be discussed further below.

5. *Hospital Policies Regarding Release.*—No indication could be found, through examination of the prerelease psychiatric interviews with patients, that there had been any relaxation of psychiatric standards for releasing 1955-1956 patients. They still had to demonstrate the absence of hyperactivity, severe mood changes, and abnormal mental content.

The administrative policies governing patient's activities prior to release did not change. Patients are granted certain amusement privileges, ground parole, and day and overnight home visits as they recover. There was no increase in the proportion of recent admissions as compared with earlier admissions, who were discharged without first having had ground parole or home visits. In fact, 1955-1956 admissions, if released, were more likely than 1953-1954 admissions to have had both ground parole and home visits prior to release.

¶ A pattern similar to that in Table 5 can be demonstrated if the *type* of hyperactivity is controlled. That is, if patients manifesting certain types of hyperactivity are taken separately—i. e., those hitting others; those threatening others; those that are anxious, shout, or run about—the 1955-1956 patients were more likely than the 1953-1954 patients to become nonhyperactive or to remain nonhyperactive. If patients are classified as hyperactive on the basis of seclusion orders rather than of the nursing notes, the same pattern appears. Moreover, the *number* of hours of seclusion of 1955-1956 patients was more likely to be reduced than that of 1953-1954 patients.

Comment

The hospital policies concerning admission and release of patients had not changed during the period under study. The social histories of the patients admitted during 1955-1956 were similar to those of patients admitted during 1953-1954. Two changes did occur, however, that may well be relevant to the improvement in release rates: desegregation and the transformation of the hospital into a quieter place, where patients are exposed to far fewer provocative incidents. The first of these, while relevant, is hardly a sufficient explanation of the improvement in release rates. There is reason to believe that the second, while probably contributing to this improvement, was not a sufficient cause either. It does not entirely explain why nonhyperactive patients showed an improvement in release rates. The hospital ward system is such that nonhyperactive patients would tend to be placed on wards with other nonhyperactive patients, and, if they changed to hyperactivity, would tend to be transferred to "disturbed" wards. Therefore, even before the advent of drug therapy, patients who had not been hyperactive at all during their first year of hospitalization or before their first release were housed in a relatively quiet, nonprovocative environment.

The most comprehensive explanation would require that we also take into account changes in the area of staff-patient relationships—more specifically arising from changes in the staff's expectations concerning patient improvement.

At least a fact from our study suggests how changes in staff-patient relationships may be initiated by changes in patient behavior. The fact is that patients who changed from hyperactivity to nonhyperactivity had a better chance for release than

TABLE 6.—*Per Cent Released Among Patients Who Changed from Hyperactivity to Nonhyperactivity, Who Remained Nonhyperactive, Who Changed from Nonhyperactivity to Hyperactivity, and Who Remained Hyperactive, by Year of Admission*

Year of Admission	Per Cent Released Among Those Who Changed from Hyperactivity to Non-hyperactivity	Number Who Changed from Hyperactivity to Non-hyperactivity	Per Cent Released Among Those Who Remained Non-hyperactive	Number Who Remained Nonhyper-active	Per Cent Released Among Those Who Changed from Nonhy-peractivity to Hyperactivity	Number Who Changed from Nonhy-peractivity to Hyperactivity	Per Cent Released Among Those Who Remained Hyperactive	Number Who Remained Hyper-active
1953	76%	37	56%	61	8%	13	13%	53
1954	57%	35	48%	61	27%	22	16%	56
1955	80%	50	73%	55	*	8	41%	29
1956	96%	25	75%	60	*	6	27%	11

* Per cent not shown because base is less than 10.

those who remained nonhyperactive.# This is true for each year, including the year prior to the advent of drug therapies (Table 6). It is likely that the change from hyperactivity connotes to staff an improvement which staff does not realize with patients who remain nonhyperactive. If so, the staff's expectation of further improvement is probably communicated back to patients who have changed and has therapeutic value toward decreasing *other* symptoms of mental illness, the absence of which is necessary for release.

Changes (1953-1956) in Staff-Patient Relationships.—From all indications, the hospital staff began to use the drugs with some reluctance:

> Our staff received these drugs initially with some considerable skepticism and lack of enthusiasm. The idea of treating psychologic illness with chemical agents is not new and in the past has invariably resulted in disappointment and disillusionment.[5]

Nevertheless, there was some indication of improvement * in patients, and by the fall of 1955 the clinical director reported[5]:

> It is too early to fully evaluate our data on the movement of our patients, but we have noted a steady, moderate decline in our average daily population. . . . If this trend is continued it may represent a most significant alteration in mental hospital operations. . . . Perhaps we will need more therapists of all types and fewer attendants who function largely as guards; more activity space . . . fewer wards with steel screens or iron bars; more social service workers and rehabilitation and vocational counselors.

Thus far the application and use of these drugs has been largely empirical. However, it may be that the "breakthrough" in psychiatry—if I may use that intriguing word with uncertain meaning—is at hand.

The lower hyperactivity of 1955-1956 patients and their higher release rate may have ensued from a change in the attitude of the staff from skepticism concerning drug therapies to a sense of expectancy that they would work. A staff relieved of many ten-

Classification of patients for Table 6 was made on the basis of whether or not they were hyperactive in either or both of two time periods. The two time periods were (1) the initial three months and (2) the remainder of the first year of hospitalization or up to first release. For example, in Table 6, of the 37 patients admitted in 1953 who were (1) hyperactive during their first three months in the hospital but (2) nonhyperactive during the remainder of their first year or up to first release, 76% were released.

If patients whose major symptom prior to hospitalization was withdrawal and if patients diagnosed as having involutional psychosis are eliminated, the pattern of Table 6 is repeated for the remainder.

* Probably the first success with the drugs was with chronic patients. In this study, treatment of 1954 first admissions did not increase the likelihood of these patients being released within their first year of hospitalization or of their being nonhyperactive over that of patients admitted for the first time prior to the use of drugs (in 1953). However, other data (not presented) did indicate that, had the period of hospitalization studied been extended beyond the first year, the release rate of 1954 patients would have exceeded that of 1953 admissions.

sions, with time freed from control of hyperactivity, with a mounting sense of hope for patient improvement, such a staff could not fail to communicate its enthusiasm to *all* patients, whether or not they were hyperactive, whether or not they were treated with drugs.

In a systematic study of chlorpromazine treatment, two St. Elizabeths psychiatrists themselves reported the optimism and enthusiasm of staff about the drugs as important to benefits from the therapy.

> The most significant result of the chlorpromazine therapy was noted in the difference of response on the two wards. This was attributed to the personalities of the nurses and attendants, since their enthusiasm for drugs varied in intensity. Patients receiving the drugs from personnel who were very enthusiastic and optimistic seemed to derive greater benefit from the medication.*†

In short, staff optimism is here suggested as the pivotal force to account for the higher 1955-1956 release rate.

Probability of Return to the Hospital

Those 1955-1956 patients who were released were more likely than were patients from earlier years to return to the hospital. This was true whether or not they had been hyperactive, and whether or not they had been treated with chlorpromazine or reserpine while in the hospital (Table 7). Incidentally, the hospital was still ahead: Thirty-nine per cent of the patients admitted in 1955-1956 had been released to the community and remained there at least one year, as compared with 32% of the patients admitted in 1953-1954.

Factors Associated with Possible Return.

In the period between release and discharge, the hospital staff itself usually dispensed the drugs, and, consequently, information about continued drug treatment was in the medical charts. There was no reliable information available concerning drug therapy beyond discharge.

Patients, who were continued ‡ on maintenance dosages of chlorpromazine or reserpine into the release period were not any more likely to stay in the community for a year than patients not so continued.

Among the released patients, a greater proportion of those admitted in 1955-1956 than of those admitted in 1953-1954 was unmarried, was Negro, or had not held a job immediately before hospitalization. Nevertheless, these changes in the com-

† The effect of staff enthusiasm during the experimental use of the drugs is also noted by Elkes[7] and Bowes.[8] A study of the physician's enthusiasm as an influence on success with chlorpromazine is reported by Feldman.[9] Another study included expectancy and enthusiasm as possible explanations for improvement in 39 out of 48 patients brought to a ward for drug treatment, the improvement appearing prior to the inception of drug treatment (Rashkis and Smarr[10]). A similar result *prior* to drug treatment is reported in another study (Wing[11]).

‡ The medical charts were not necessarily a reliable source to determine whether patients *took* the drugs they were given, though most patients and their relatives were interviewed during the release period about whether or not the patient actually was taking the drugs, if prescribed.

TABLE 7.—*Per Cent of Released Patients Returning to the Hospital, Who Had Been Hyperactive or Nonhyperactive and Who Had Been Treated with Drugs While in the Hospital, by Year of Admission*

	Hyperactive Patients				Nonhyperactive Patients					
Year of Admission	Per Cent Returned Among Treated	Number Treated	Per Cent Returned Among Not Treated	Number Not Treated	Per Cent Returned Among Treated	Number Treated	Per Cent Returned Among Not Treated	Number Not Treated	All Released: Per Cent Returned	All Released: Number Released
1953			19%	36			15%	34	17%	70
1954	36%	14	24%	21	*	1	14%	28	21%	64
1955-1956 †	46%	68	*	8	43%	51	32%	25	41%	152

* Per cent not shown because base is less than 10.

† Excludes patients released after Oct. 31, 1956, for whom a year had not yet elapsed at the time data collection was discontinued, Oct. 30, 1957.

TABLE 8.—*Per Cent of Released Patients Returning to the Hospital, Grouped by Whether or Not They Held a Job at Admission, by Year of Admission*

Year of Admission	Per Cent Returned Among Patients with Jobs	Number of Patients with Jobs	Per Cent Returned Among Patients Without Jobs	Number of Patients Without Jobs
1953	13%	24	20%	30
1954	16%	25	22%	27
1955-1956 *	32%	42	48%	69

* Excludes patients released after Oct. 31, 1956, for whom a year had not yet elapsed at the time data collection was discontinued, Oct. 31, 1957.

position of the population of *released* patients did not account for the increased probability that 1955-1956 patients would return to the hospital. The probability of return of released 1955-1956 patients was greater than that of the return of released 1953-1954 patients for both those with jobs and those without jobs at the time of admission (Table 8), for those married and those unmarried (Table 9), and for Negroes and whites (Table 9).

In general, the conditions faced on release about which we had information did not account for why 1955-1956 patients, if released, were more likely to return to the hospital than were 1953-1954 patients. Alternative explanations would be either (1) *other* conditions external to the hospital or (2) a condition supportive of the patient's recovery singular to the hospital, and therefore not existing in the community.

The optimism of the staff concerning patient recovery has been suggested as the condition, missing or diminutive in 1953-1954, which increased the probability of release for 1955-1956 admissions. Staff optimism arose because the hospital witnessed within a relatively short time a dramatic improvement in the usual behavior of its patient population. The families or friends of released patients had no similar institutional experience. It is plausible that if an additional proportion of 1955-1956 patients recovered because of staff optimism, these additional patients were likely to relapse, once released, because they were no longer sustained by staff optimism.

Summary and Conclusions

The findings show that patients recently hospitalized for the first time (1955-1956), whether or not they were treated with chlorpromazine or reserpine, were more likely to be released to the community than were patients hospitalized for the first time before the use of drugs (1953).

Hyperactivity is considered the most positive indicator for drug treatment. Nevertheless, nonhyperactive and nontreated hyperactive patients shared in the sharply increased chance for release during the recent drug treatment period.

During the years studied there were no changes in hospital admission and release procedures. Nor were there any substantial changes in the diagnostic categories, symptomatology, or previous social histories of patients entering the hospital. Desegregation, beginning in the latter part of 1954,

TABLE 9.—*Per Cent of Released Patients Returning to the Hospital Within Race-Sex Groups by Marital Status, by Year of Admission* *

Year of Admission	White Males			White Females			Negro Males			Negro Females		
	Married	Unmarried †	Total	Married	Unmarried †	Total	Married	Unmarried †	Total	Married	Unmarried †	Total
1953-1954	0%	‡	5%	28%	8%	19%	‡	9%	6%	32%	18%	27%
	N-10	N-9	N-19	N-29	N-24	N-53	N-6	N-11	N-17	N-28	N-17	N-45
1955-1956 §	‡	‡	36%	39%	42	41%	‡	37%	37%	37%	50%	44%
	N-5	N-9	N-14	N-23	N-26	N-49	N-3	N-24	N-27	N-27	N-36	N-63

* N in this table indicates the number of released patients who fall into the particular subgroup.

† Includes single, separated, divorced, widowed, and common-law.

‡ Per cent not shown because base is less than 10.

§ Excludes patients released after Oct. 31, 1956 for whom a year had not yet elapsed at the time data collection was discontinued, Oct. 31, 1957.

does not seem a plausible explanation of the extent and sharpness of change in probability of release. The decrease in provocative behavior coincident with the extensive use of chlorpromazine and reserpine may have been important to decreasing the hyperactivity of patients on "disturbed" wards, but it does not seem reasonable to account for the enhanced chance for release of patients not hyperactive at any time within the period studied.

A more comprehensive hypothesis would be that the increasingly optimistic expectation of staff that patients would recover had increased the probability that *all* patients, whether hyperactive or not, whether treated with drugs or not, would, in fact, recover. This optimism incidentally did not necessarily derive from the results of drug therapy with patients admitted for the first time in 1954; it may well be based on success with chronic patients.

It was further suggested that the discontinuity in optimism between hospital and community explains why the recent admissions, if released, have been more likely to return to the hospital within one year than had earlier admissions.

Laboratory of Socio-Environmental Studies, National Institute of Mental Health (14).

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Announcements

The ARCHIVES OF NEUROLOGY AND PSYCHIATRY was first published in 1919. At that time neurology and psychiatry were considered related subject fields and it was thought one journal would serve both adequately.

Over the years, psychiatry has been emerging as a distinct specialty. The volume of literature has increased to such an extent that official publications reporting psychiatry either could not absorb it or felt the need to condense the material to accommodate more contributions. Psychiatrists began to feel also that the ARCHIVES OF NEUROLOGY AND PSYCHIATRY should allot more space to psychiatry, that its emphasis over the years had been neurological.

In July, 1956, an effort was made to give equal emphasis to both neurology and psychiatry by dividing the ARCHIVES OF NEUROLOGY AND PSYCHIATRY into a two-section journal, with an editorial board for the Section on Neurology and a separate board for the Section on Psychiatry. This division had the effect of reducing the number of pages devoted to neurology, and the result was late publication dates for accepted articles, with the natural development of a large backlog. More psychiatric manuscripts were now submitted to the ARCHIVES, and only very high editorial standards and a high rate of rejection prevented a large backlog from forming.

The final development is to publish two separate journals. The division is prompted by the demand by both neurologists and psychiatrists for more text pages; by the neurologists, who feel the quality of a journal devoted exclusively to neurology can be much improved, and by the psychiatrists, who believe it is more realistic to recognize neurology and psychiatry as distinct clinical specialties. Consequently, July, 1959, will see the introduction of these two journals—the *A. M. A. Archives of Neurology* and the *A. M. A. Archives of General Psychiatry*.

Books

BOOK REVIEWS

Schizophrenia: A Review of the Syndrome. Edited by Leopold Bellak, M.D., with the collaboration of Paul K. Benedict, M.D. Price, $14.75. Pp. 1,010. Logos Press, Inc., Box 273, Cooper Station, New York, 1958.

It is impossible to comment in detail on a review of over a thousand pages of collected material on such a huge subject, but this monumental work should not be neglected without appropriate notice. In addition to the text, the book contains 4,442 references and 59 pages of detailed author and subject indices.

Ten years ago Bellak reviewed the literature from 1936 to 1946 under the title of "Dementia Praecox." The present book reviews the literature from 1946 to 1956, with slight overlapping. The editor believes that there are many schizophrenias and that there are many causes and cures. He states: "It is hoped that the either/or, single organic factor, descriptive or nebulous psychodynamic notions of schizophrenia will eventually give way to a carefully conceptualized and experimentally verified concept of a multiple-factor, psychosomatic-genetic, ego psychological syndrome . . . which will adequately explain all of the clinical contingencies one may encounter." To this we add our own hopes and our gratitude to Bellak, because his endeavors have and will help us to attain this goal. The book is a must for personal and institutional libraries.

ROY R. GRINKER, M.D.

Operational Values in Psychotherapy. By Donald D. Glad, Ph.D. No price stated. Pp. 326. Oxford University Press, 114 Fifth Ave., New York 11, 1959.

The author presents the reader with a discussion of four methods of psychotherapy: Freud's psychoanalysis; Sullivan's interpersonal psychiatry; Rank's dynamic relationship therapy, and Rogers' phenomenology, viewed in operational form. He contends that psychotherapy theories define the therapist's methods and define the personality structures as viewed by the therapist, have characteristic effects in determining the structure of the patient's process of change, and are important in evaluating the determinance of change. The arguments that the author uses are extremely clear and are exemplified by case vignettes. Each of the four main therapeutic techniques is compared with the others, and the operational and theoretical notions of each system are integrated so that the relationships of theory, operations, and the patient's experiences of change are adequately documented. This book is a welcome addition to the writings of persons dissatisfied with the all-embracing notions of specific schools of psychotherapy. There is clear evidence that theory and operations are closely linked. What happens to a patient depends largely, then, on the type of therapist to whom he goes in respect to his affiliation with one or another of the four schools exemplified by Dr. Glad, who, of course, could have considered other theoretical systems as well. However, perhaps the others are not so sharply defined as the four which he discusses. What is missing in this book, it seems to the reviewer, is the positive postulation of a kind of therapy which is based on operational theory rather than on dynamic theory. Perhaps one could neglect theoretical psychodynamics and view the living, suffering patient purely operationally in an effort to exchange information and to correct errors in communication which have nothing to do with preconceived theory. Perhaps some day we can develop such a system of therapy that is much more open and not biased by theory, although, as Dr. Glad has pointed out, at present this is only rarely found to be the case. It is suggested that this book is a valuable source of information regarding the theory and operations of the four schools which Dr. Glad has chosen. It will not teach the reader how to do the various therapies, but, as he states in the first sentence of his preface: "You can no more master psychotherapy by reading only, than win a woman with your eyes alone." Perhaps by reading Dr. Glad's book the psychotherapist and the teacher of psychotherapy will become more aware of what the therapist puts into the therapeutic situation over and above what it warrants, how the therapist places his bias and preconceptions which often limit or, at the worst, interfere

with the psychotherapeutic process. This book has an adequate bibliography and a very good index and is highly recommended.

ROY R. GRINKER, M.D.

Current Concepts of Positive Mental Health. By Marie Jahoda. Price, $2.75. Pp. 136. Basic Books, Inc., 54 Fourth Ave., New York, 1958.

This is the first of a series of books derived from a national mental health survey by a Joint Commission on Mental Illness and Health and supported by the national government through grants authorized by Congress to the National Institute of Mental Health and from some private sources. It is expected that ten monographs will be published in time, followed by a final report, with a summary of findings and recommendations for national and state mental health programs. Certainly this first volume augurs well for the total series, because the author has presented the problems of mental health in succinct and scientific style, with extremely worth-while suggestions for future research.

The author starts out with the assumption that mental health is not the negative of mental illness. It suggests that there is a condition that could be called positive mental health, and this the author takes as her focus for research. If funds are to be raised and expended to promote mental health, then a useful concept of this condition should be established. It becomes obvious at once that the evaluation of actions as sick or normal depends upon accepted social conventions and, therefore, on the culture in which these actions are being viewed.

Dr. Jahoda classifies six major categories of concepts or approaches to the notion of mental health, as follows: 1. It is suggested that indications of positive mental health should be sought in the attitudes of an individual toward himself. 2. The individual's style and degree of growth, development, or self-actualization are expressions of mental health. 3. Emphasis has been placed on a central integrative function which incorporates the aspects of the first two headings. 4. Autonomy, which indicates an individual's degree of independence from social influences. 5. Many have proposed that mental health is manifested in the adequacy of an individual's perception of reality. 6. Some persons have suggested that mastery of the environment may be used as a criterion for mental health.

The author then discusses in considerable detail each one of the above headings and breaks them down into their component parts. Finally, she takes the various ideas which have been related to these various points of view and discusses how they can be dealt with in systematic research. She states that the complex problems of mental health will be solved not by exhortations and pious hopes but through the further investigations into the actual facts, which are extremely slow and costly to accumulate.

At the end of the book there is a chapter entitled "Viewpoint of the Clinician," by Walter E. Barton. It incorporates the notion that health is a product of disease prevention and treatment and with illness forms a continuum. Dr. Barton objects to the viewpoint as expressed in this book that there is a positive mental health. The data used to further his point are largely several quotations from various writers in the field. The chapter appears to the reviewer to be redundant, and not at all helpful to the author's attempts to place our concepts of mental health on a sound scientific basis.

Dr. Jahoda's contribution is excellent and should be read in detail by clinicians, investigators, and by the intelligent lay person who is in any way involved with the problems of mental health and illness.

ROY R. GRINKER, M.D.

Mental Subnormality. By Richard L. Masland, Seymour B. Sarason, and Thomas Gladwin. Price, $6.75. Pp. 442. Basic Books Inc., 59 Fourth Ave., New York 3, 1958.

Few of us realize that of the 4,200,000 children born annually in the United States, 142,800 will never achieve an intellect exceeding that of the 12-year-old child. In its sobering magnitude, this figure amply justifies the efforts of the authors of "Mental Subnormality" to review and integrate the known facts pertaining to retardation and to define pivotal points around which future research in this area may center. Under the auspices of the National Association for Retarded Children, Masland, Sarason, and Gladwin bring to the reader a panoramic and sweeping view of a large number of studies in mental retardation. Often they pause in their review to call attention to the conceptual, methodological and attitudinal problems that stand in the way of the increased understanding of the subnormal

individual. Thus, their scholarly review constitutes an excellent reference volume for the researcher in neurology, biochemistry, endocrinology, psychiatry, and psychology.

The plan of the volume divides mental subnormality into two major areas: problems of prevention and the examination of the cultural and psychological difficulties affecting the mentally handicapped. Post- and prenatal causes, as well as perinatal influences, are discussed from a number of vantage points, with primary focus on genetic and environmental factors in the pathology of the nervous system. Attention is given to certain relationships between the age of the parents and the condition of the infant, as well as to dietary habits of the mother, since these seem to bear on the eventual mental state of the baby. The authors are keenly aware of the complexity of the research problems encountered, regardless of what specific medical specialty one chooses as a framework. This awareness prompts them to frequent pleas for multidisciplinary research. Specifically, they argue for the establishment of more research centers attached to training schools and custodial institutions. The need for interdisciplinary research is emphasized so fervently that one is left with the impression that scientists in the area of retardation are as isolated from one another as are the mentally retarded from the main stream of human interchange.

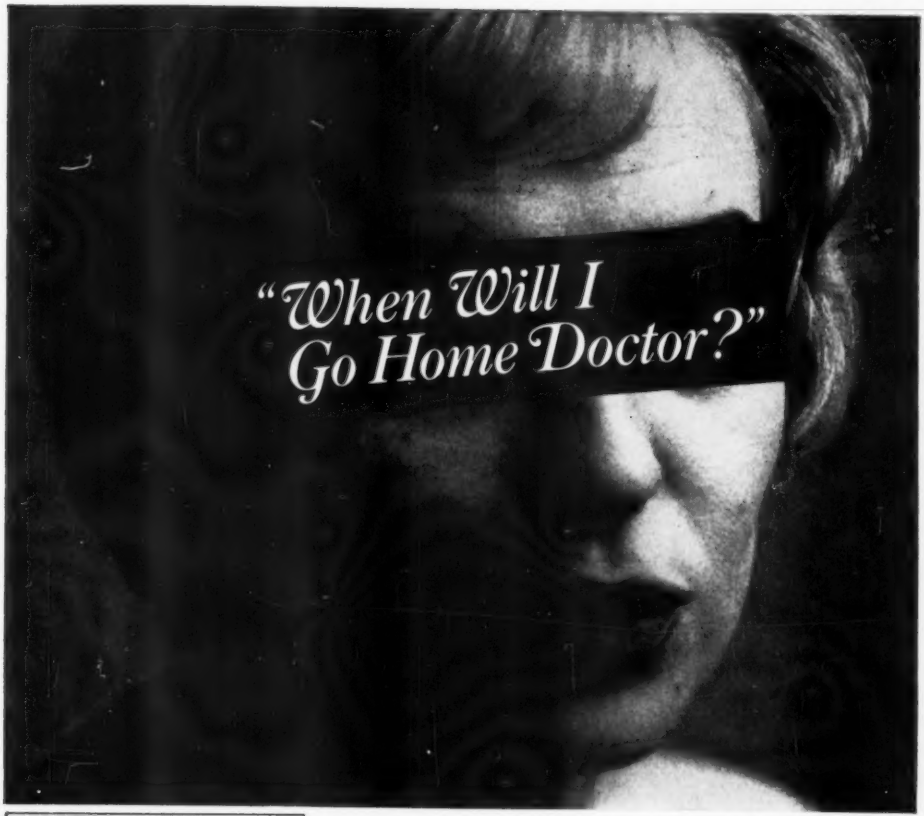
Because the first section of the book deals with the problem of prevention in the general area of genetic, endocrinological, neurological, and nutritional studies, it is much more tightly written and organized than is the second section of "Mental Subnormality." In discussing the medical areas of research, the line between fact and speculation is fairly clearly drawn. However, once the authors embark on the exploration of social, cultural, and psychological studies of retardation, there is a rather noticeable change in pace and tone. The reader is then led into vast regions, the boundaries of which are sometimes vague and overlapping. The authors wrestle bravely with the amorphous aggregate of variables that may possibly explain why 716,000 subnormal individuals between the ages of 18 and 37 were rejected from military service during World War II. They devote 20 laborious pages to the discussion of various possible explanations, only to plunge the reader into serious doubt over the validity of intelligence tests, and they do not succeed in clarifying the concept of intelligence quotient.

Although a great many intelligence tests are mentioned, the authors do not find much merit in any of them because "there is no evidence or justification for the assumption that the problem solving tasks sampled by these tests are representative of problem solving behavior in everyday life" (page 183). The examination of tests continues with the implicit assumption that a "culture-free" intelligence test could be devised; this would be scientifically and practically most valuable. One may well take issue with the practical usefulness of such a hypothetical "culture-free" tests, since predictions from test data invariably concern the individual in his milieu, not in a cultural vacuum.

For the clinician in psychiatric practice the most valuable parts of the book are undoubtedly those concerned with the problems of differentiation between psychosis and mental deficiency and brief but hard-hitting remarks about psychotherapy for the retarded individual. The problem of the diagnosis of minimal brain injury through psychological tests is put in terms of the unreliable criterion provided by neurological examinations of children. There is stern warning in the highlighting of the diagnostic pitfall: When a child is labeled retarded, psychodynamics receive little attention, and all the peculiarities of his behavior are attributed to his low I. Q. The therapeutic efforts of Itard and Witmer with "very young, withdrawn, autistic-like and defective-like" children receive special attention. The review of the writings of these pioneers raises the question whether it is not the making public of personal experience between clinician and patient—in its minutest and most sensitive details—that is more likely to serve as a road to understanding than a priori theoretical formulations, no matter how elegant they may be. The authors point an accusing finger at our profession by reminding the reader of the almost complete "absence of intensive, psychoanalytic studies of subnormal individuals" and attribute the present state of affairs to disinterest on the part of psychoanalytically trained therapists.

In closing, "Mental Subnormality" offers a number of suggestions for furthering research. It can only be hoped that the authors' recommendations will not fall on deaf ears.

MARY ENGEL, PH.D.



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Klimczynski, J.J.T.: Treatment of Chronically Ill Psychotic Patients with Trifluoperazine: A Preliminary Report, *ibid.*, pp. 101-112.

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Goldman, D.: Clinical Experience with Trifluoperazine: Treatment of Psychotic States, *ibid.*, pp. 71-86.

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Focal Jacksonian	19	19 (100%)		

Results in 835 epileptic patients who had failed to respond successfully to other anticonvulsants. "Mysoline" was added to current medication which, in some cases, was eventually replaced by "Mysoline" alone.

Type of Seizure	Number of Patients	Completely Controlled	50-90% Improved	<50%
Grand Mal	613	175 (28.5%)	253 (41.2%)	185 (30.3%)
Psychomotor	130	10 (7.7%)	65 (50%)	55 (42.3%)
Focal Jacksonian	92	14 (15.2%)	36 (39.1%)	42 (45.7%)

The dramatic results obtained with "Mysoline" advocate its use as a preparation of choice for effective and well tolerated therapy in the control of grand mal and psychomotor attacks.

SUPPLIED: 0.25 Gm. scored tablets, bottles of 100 and 1,000.

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References: 1. Vorbusch, H. J.: J. Clin. & Exper. Psychopath., (Jan.-Mar.) 1959. 2. Feldman, P. E.: Am. J. Psychiat. *115*:736 (Feb.) 1959.

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